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=> d his

     (FILE 'HOME' ENTERED AT 12:56:14 ON 06 AUG 2001)

     FILE 'HCAPLUS' ENTERED AT 12:56:19 ON 06 AUG 2001

     FILE 'REGISTRY' ENTERED AT 12:56:54 ON 06 AUG 2001
L1             1 S 81627-83-0
L2             0 S S 143011-72-7
L3             1 S 143011-72-7
L4             1 S 83869-56-1
L5             3 S L1  OR L3 OR L4

     FILE 'HCAPLUS' ENTERED AT 12:58:22 ON 06 AUG 2001
L6         12161 S L5
L7          7634 S GM CSF OR GRANULOCYTE MACROPHAGE COLONY STIMULAT? FACTOR#
L8         12527 S L6 OR L7
L9          3034 S TUMOR ASSOC? (L) ANTIGEN#
L10          158 S L8 AND L9
L11        27946 S VACCINE#
L12        46101 S ANTITUMOR AGENT#
L13           92 S L10 AND L11
L14           50 S L13 AND L12
L15            0 S PROLIFERATION IMCOMP?
L16            0 S PROLIFERATION INMCOMP?
L17            3 S PROLIFERATION INCOMP?
L18            1 S (PROLIFERATION INCOMP?)/AB
L19            3 S L17 OR L18
L20            2 S L14 AND L19
L21        90945 S MOL? (3A) (WT# OR WEIGHT#)
L22            2 S L21 AND L14
L23            3 S L22 OR L20
L24       274679 S (250 OR 160 OR 150 OR 130 OR 105 OR 60 OR 32 OR 31 OR 27 OR
2
L25           41 S L24 AND  L13
L26           19 S L24 AND  L14
L27         5549 S L24 AND (L21 OR MOL? (2W) (WT OR WEIGHT#))
L28            2 S L14 AND L27
L29       151819 S KDA OR KD OR KDS OR KDA/AB OR KD/AB OR KDS/AB OR
KILODALTON#
L30         7647 S L24 AND L29
L31            0 S L30 AND L14
L32            3 S L28 OR L23
L33        19728 S PROSTAT?
L34           10 S L14 AND L33
L35           10 S L34 OR L32
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=> fil reg

FILE 'REGISTRY' ENTERED AT 13:11:53 ON 06 AUG 2001
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:    5 AUG 2001  HIGHEST RN 350479-72-0
DICTIONARY FILE UPDATES:   5 AUG 2001  HIGHEST RN 350479-72-0

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.

=> d que l5

L1            1 SEA FILE=REGISTRY ABB=ON  81627-83-0
L3            1 SEA FILE=REGISTRY ABB=ON  143011-72-7
L4            1 SEA FILE=REGISTRY ABB=ON  83869-56-1
L5            3 SEA FILE=REGISTRY ABB=ON  L1 OR L3 OR L4


=> d l5 rn cn 1-3


L5   ANSWER 1 OF 3  REGISTRY  COPYRIGHT 2001 ACS
RN   143011-72-7  REGISTRY
CN   Colony-stimulating factor, granulocyte (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   G-CSF
CN   Granocyte
CN   Granulocyte colony-stimulating factor

L5   ANSWER 2 OF 3  REGISTRY  COPYRIGHT 2001 ACS
RN   83869-56-1  REGISTRY
CN   Colony-stimulating factor 2 (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Colony-stimulating factor II
CN   CSF 2
CN   GM-CSF
CN   Granulocyte-macrophage colony-simulating factor
CN   Granulocyte-macrophage colony-stimulating activity
CN   Granulocyte-macrophage colony-stimulating factor
CN   Granulocyte-macrophage-inducing factor
CN   Granulocyte-monocyte colony-stimulating factor
CN   Macrophage-granulocyte CSF
CN   Macrophage-granulocyte-colony-stimulating factor

L5   ANSWER 3 OF 3  REGISTRY  COPYRIGHT 2001 ACS
RN   81627-83-0  REGISTRY
CN   Colony-stimulating factor 1 (9CI)  (CA INDEX NAME)
OTHER NAMES:
```

CN CSF 1
CN Cytokines, macrophage colony-stimulating factor
CN Lymphokines, macrophage colony-stimulating factor
CN M-CSF
CN Macrophage colony-stimulating factor
CN Macrophage-monocyte colony-stimulating factor
CN Monocyte colony-stimulating factor

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 13:12:07 ON 06 AUG 2001
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FILE COVERS 1947 - 6 Aug 2001 VOL 135 ISS 7
FILE LAST UPDATED: 5 Aug 2001 (20010805/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGlstRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d his l6-

(FILE 'REGISTRY' ENTERED AT 12:56:54 ON 06 AUG 2001)

FILE 'HCAPLUS' ENTERED AT 12:58:22 ON 06 AUG 2001
L6 12161 S L5
L7 7634 S GM CSF OR GRANULOCYTE MACROPHAGE COLONY STIMULAT? FACTOR#
L8 12527 S L6 OR L7
L9 3034 S TUMOR ASSOC? (L) ANTIGEN#
L10 158 S L8 AND L9
L11 27946 S VACCINE#
L12 46101 S ANTITUMOR AGENT#
L13 92 S L10 AND L11
L14 50 S L13 AND L12
L15 0 S PROLIFERATION IMCOMP?
L16 0 S PROLIFERATION INMCOMP?
L17 3 S PROLIFERATION INCOMP?

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L18           1 S (PROLIFERATION INCOMP?)/AB
L19           3 S L17 OR L18
L20           2 S L14 AND L19
L21       90945 S MOL? (3A) (WT# OR WEIGHT#)
L22           2 S L21 AND L14
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L25          41 S L24 AND  L13
L26          19 S L24 AND  L14
L27        5549 S L24 AND (L21 OR MOL? (2W) (WT OR WEIGHT#))
L28           2 S L14 AND L27
L29      151819 S KDA OR KD OR KDS OR KDA/AB OR KD/AB OR KDS/AB OR
KILODALTON#
L30        7647 S L24 AND L29
L31           0 S L30 AND L14
L32           3 S L28 OR L23
L33       19728 S PROSTAT?
L34          10 S L14 AND L33
L35          10 S L34 OR L32

     FILE 'REGISTRY' ENTERED AT 13:11:53 ON 06 AUG 2001

     FILE 'HCAPLUS' ENTERED AT 13:12:07 ON 06 AUG 2001

=> d .ca 135 1-10


L35  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:416979  HCAPLUS
DOCUMENT NUMBER:          135:45169
TITLE:                    Characterization of cancer-associated antigen
OY-TES-1
INVENTOR(S):              Ono, Toshiro; Nakayama, Eiichi
PATENT ASSIGNEE(S):       Ludwig Institute for Cancer Research, USA
SOURCE:                   PCT Int. Appl., 127 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2001040271      A2   20010607      WO 2000-US32750  20001201
         W:  AU, CA, CN, JP, KR, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
PRIORITY APPLN. INFO.:                    US 1999-168353   P  19991201
                                          US 2000-559013   A  20000426
```

AB The authors disclose the identification of OY-MC-4 cancer/testis antigen expressed in methylcholanthrene-induced fibrosarcoma cancer cells using antisera from mice bearing such tumors. Using primers specific for the mouse OY-MC-4 antigen, the authors performed homol. searching of a human testis cDNA library. The results identified the human homolog designated OY-TES-1 which encoded the proacrosin-binding protein sp32. Using a recombinant antigen, the authors demonstrate the presence of an antibody

response to OY-TES-1 assocd. with several human tumors. Fragments of the foregoing including functional fragments and variants also are provided. Kits contg. the foregoing mols. addnl. are provided. The mols. provided by the invention can be used in the diagnosis, monitoring, research, or treatment of conditions characterized by the expression of one or more cancer assocd. antigens.

IC ICM C07K014-00
CC 15-2 (Immunochemistry)
Section cross-reference(s): 1, 2, 14
IT Interleukins
Saponins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as adjuvant for tumor antigen **vaccine**)
IT Bladder
Mammary gland
Prostate gland
(neoplasm; gene expression for OY-TES-1 antigen in)
IT **Antigens**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**; diagnosis of cancer by detection of)
IT **Vaccines**
(tumor; cancer antigen and genetic immunization for)
IT **Antitumor agents**
(**vaccines**; cancer antigen and genetic immunization for)
IT **83869-56-1, GM-CSF**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as adjuvant for tumor antigen **vaccine**)

L35 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:152726 HCAPLUS
DOCUMENT NUMBER: 134:206569
TITLE: Human CTLA-4 antibodies and their uses
INVENTOR(S): Korman, Alan J.; Halk, Edward L.; Lonberg, Nils
PATENT ASSIGNEE(S): Medarex, Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014424	A2	20010301	WO 2000-US23356	20000824

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-150452 P 19990824
AB The present invention provides novel human sequence antibodies against

human CTLA-4 and methods of treating human diseases (e.g. cancer, allergy,
inflammation, autoimmune disease, graft vs. host disease, Alzheimer's disease), infections and other conditions using these antibodies.
IC ICM C07K016-00
CC 15-3 (Immunochemistry)
Section cross-reference(s): 1, 3, 63
ST monoclonal antibody heavy light chain CTLA4; infection cancer inflammation
allergy antibody CTLA4; autoimmune graft vs host disease **vaccine**
IT Dendritic cell
(antigen-loaded **vaccine**; human CTLA-4 antibodies and their uses)
IT Neoplasm
(cell **vaccine**; human CTLA-4 antibodies and their uses)
IT Allergy
Alzheimer's disease
Amyloidosis
Animal cell line
Animal virus
Antitumor agents
Autoimmune disease
B cell (lymphocyte)
Bacteria (Eubacteria)
Chemotherapy
DNA sequences
Fungi
Human immunodeficiency virus
Hybridoma
Immunosuppressants
Infection
Inflammation
Kidney, neoplasm
Melanoma
Molecular cloning
Mycosis
Parasite
Pathogen
Protein sequences
T cell (lymphocyte)
Transplant rejection
Vaccines
(human CTLA-4 antibodies and their uses)
IT **Prostate** gland
(neoplasm; human CTLA-4 antibodies and their uses)
IT **Antigens**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**; human CTLA-4 antibodies and their uses)
IT **Vaccines**
(tumor; human CTLA-4 antibodies and their uses)
IT **Antitumor agents**
(**vaccines**; human CTLA-4 antibodies and their uses)
IT **83869-56-1, GM-CSF**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(-modified tumor cell **vaccine**; human CTLA-4 antibodies and their uses)

L35 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:101291 HCAPLUS
DOCUMENT NUMBER: 134:161880
TITLE: cDNAs encoding the Flt-3 receptor ligand and there use
as adjuvants in vector **vaccines**
INVENTOR(S): Hermanson, Gary George
PATENT ASSIGNEE(S): Vical Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009303	A2	20010208	WO 2000-US20679	20000731

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-146170 P 19990730

AB A method of increasing the strength of the immune response of vector vaccines using an expression vector for the Flt3 ligand is described. The vaccines are made of independent non-integrating expression vectors: one encodes the antigen or a cytokine and the other encodes the Flt3 ligand. The present invention also provides a method broadly directed to improving immune response of a vertebrate in need of immunotherapy by administering in vivo, into a tissue of a vertebrate, a Flt-3 ligand-encoding polynucleotide and one or more antigen- or cytokine-encoding polynucleotides. The polynucleotides are incorporated into the cells of the vertebrate in vivo, and a prophylactically or therapeutically effective amt. of a Flt-3 ligand and one or more antigens is produced in vivo.

IC ICM C12N015-00
CC 15-2 (Immunochemistry)
Section cross-reference(s): 3
ST Flt3 ligand gene adjuvant vector **vaccine**
IT Lymphoma
(B-cell, antigens of, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Hemopoietins
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FLT3 ligand; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Immunotherapy
(Flt-3 receptor ligand as adjuvant in; cDNAs encoding Flt-3 receptor

ligand and there use as adjuvants in vector **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GM2, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GP100, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GloboH, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Genetic element
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IRES (internal ribosomal entry site) element, in polycistronic vector **vaccine** constructs; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(KSA, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LeIF (Leishmania initiation factor), gene for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Blood-group substances
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Ley, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MAGE1, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MAGE2, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MUC2, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MUC3, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Antigens

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MUC4, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MUC5AC, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MUC5B, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MUC7, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PSCA, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PSMA, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Chemokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SDF-1 (stromal-derived factor-1), gene for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TRP1, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TRP2, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Thomsen-Friedenreich, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Blood-group substances
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Tn, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Absidia
Acanthocheilonema
Acremonium

Actinomyces
Adenoviridae
Aelurostrongylus
Alphavirus
Alternaria
Ancylostoma
Angiostrongylus
Ant (Formicidae)
Aphthovirus
Ascaris
Aspergillus
Babesia
Bacillus (bacterium genus)
Bacteroides
Balantidium
Bartonella
Basidiobolus
Besnoitia
Bipolaris
Blackfly
Blastomyces
Bordetella
Borrelia
Brucella
Brugia
Bunostomum
Calicivirus
Campylobacter
Candida
Canine distemper virus
Capillaria (nematode)
Capnocytophaga
Chabertia
Chlamydia
Cimex lectularius
Clostridium
Coccidioides
Conidiobolus
Cooperia
Coronavirus
Corynebacterium
Coxiella
Crenosoma
Cryptococcus (fungus)
Cryptosporidium
Curvularia
Dermatophilus
Dictyocaulus
Dioctophyme
Dipetalonema
Diphyllobothrium
Diplopylidium
Dirofilaria
Dracunculus (worm)
Ebola virus
Ehrlichia
Eimeria

Encephalitozoon
Entamoeba
Enterobius
Enterococcus
Enterovirus
Epidermophyton
Escherichia
Exophiala
Feline infectious peritonitis virus
Filaroides
Flaviviridae
Flea (Siphonaptera)
Francisella
Fusobacterium
Geotrichum
Giardia
Gnat
Haematobia irritans
Haemobartonella
Haemonchus
Haemophilus
Hammondia
Helicobacter
Hepadnaviridae
Hepatozoon
Herpesviridae
Histoplasma
Human coxsackievirus
Human immunodeficiency virus
Human parainfluenza virus
Influenza virus
Isospora
Klebsiella
Lagochilascaris
Leishmania
Leptospira
Listeria
Loa
Louse
Madurella
Malassezia
Mansonella
Marburg virus
Microsporidia
Microsporum
Mite and Tick
Moniliella
Mortierella
Mosquito
Mucor
Muellerius
Mycobacterium
Mycoplasma
Nanophyetus
Necator
Neisseria
Nematodirus

Neorickettsia
Neospora
Nocardia
Nosema
Oesophagostomum
Onchocerca
Opisthorchis
Orthomyxovirus
Ostertagia
Paecilomyces
Papillomavirus
Parafilaria
Paragonimus
Paramyxovirus
Parascaris
Parasite
Parasitic worm
Parvovirus
Pasteurella
Penicillium
Pentatrichomonas
Peptococcus
Peptostreptococcus
Pestivirus
Phialemonium
Phialophora
Physaloptera
Picornaviridae
Plasmodium (malarial genus)
Pneumocystis
Poxviridae
Proteus (bacterium)
Protoplast and Spheroplast
Protostrongylus
Prototheca
Protozoa
Pseudallescheria
Pseudomicrodochium
Pseudomonas
Pythium
Rabies virus
Reoviridae
Respiratory syncytial virus
Retroviridae
Rhinosporidium
Rhinovirus
Rhizopus
Rickettsia
Rotavirus
Salmonella
Sandfly
Sarcocystis
Schistosoma
Scolecobasidium
Setaria (nematode)
Shigella
Spider

Spirocerca
Sporothrix
Staphylococcus
Stemphylium
Stephanofilaria
Stomoxys calcitrans
Streptococcus
Streptococcus pneumoniae
Strongyloides
Strongylus
Tabanidae
Theileria
Thelazia
Toxascaris
Toxocara
Toxoplasma
Treponema
Triatominae
Trichinella
Trichophyton
Trichosporon
Trichostrongylus
Trichuris
Trypanosoma
Tsetse fly (Glossina)
Uncinaria
Wuchereria
Xylohypha
Yersinia
(adjuvants for vector **vaccines** against; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Carcinoembryonic antigen
Epidermal growth factor receptors
Prostate-specific antigen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Immunostimulants
(adjuvants, Flt-3 receptor ligand as; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Blood
Bone
Bone marrow
Brain
Cartilage
Connective tissue
Eye
Gallbladder
Gland
Heart
Intestine
Kidney
Liver
Lung
Lymph

Mucous membrane
Muscle
Nervous system
Ovary
Pancreas
Skin
Spleen
Stomach
Testis
Thymus gland
Tongue
Uterus
(administration of vector **vaccines** to; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Antibodies
(anti-idiotypic, to B cell lymphoma, vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic, in delivery of vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Mucins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(episialins, MUC1, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in
vector **vaccines**)

IT Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments, as antigens, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion products, const. regions, as antigen, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Interleukin 10
Interleukin 12
Interleukin 15
Interleukin 18
Interleukin 2
Interleukin 3
Interleukin 4
Interleukin 5
Interleukin 6
Interleukin 7
Interleukin 8
Macrophage inflammatory protein 1.alpha.
Macrophage inflammatory protein 1.beta.
RANTES (chemokine)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Cytokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genes for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Neuroglia
(glioma, **vaccines** against; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interferon .omega., gene for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Animal virus
(leukemia, for vector **vaccines** against; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Chemokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monocyte chemoattractant protein 3, gene for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Fly (Diptera)
(myiasis, adjuvants for vector **vaccines** against; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Intestine
(rectum, administration of vector **vaccines** to; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Muscle
(smooth, administration of vector **vaccines** to; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT **Vaccines**
(synthetic; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Chemotherapy
Gene therapy
Radiotherapy
Surgery
(treatment of cancer with **vaccines** and; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Animal virus
(tumor, adjuvants for vector **vaccines** against; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT **Vaccines**
(tumor; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)
IT Lymphoma

Melanoma
(**vaccines** against; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT **Antitumor agents**
(**vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Fungi
(zoopathogenic, adjuvants for vector **vaccines** against; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.tau., gene for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha., gene for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta., gene for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Transforming growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-, gene for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT neu (receptor)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-chain, as antigen, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma., gene for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT 153132-93-5 156287-68-2 156287-70-6 159964-80-4 171404-15-2
183972-05-6, Flt3 ligand (mouse isoform T169 precursor) 253862-43-0
324574-06-3 324574-07-4 324574-08-5 324830-56-0 324830-57-1
324830-58-2 324830-59-3 324830-60-6 324830-61-7 324830-62-8
324830-63-9 324830-64-0 324830-65-1 324830-66-2 324830-67-3
324830-68-4 324830-69-5
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT 9002-10-2, Tyrosinase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as antigen, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT 11096-26-7, Erythropoietin 62683-29-8, CSF **81627-83-0**, M-CSF **83869-56-1**, **GM-CSF 143011-72-7**,

G-CSF
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene for, in vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT 9002-61-3, Gonadotropin, chorionic
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human .beta.-chain, as antigen, adjuvants for vector **vaccines** using gene for; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT 2462-63-7, DOPE 20255-95-2, DMPE 153312-64-2, DMRIE 201036-16-0, DPyPE 208040-06-6, GAP-DLRIE 299207-54-8, GAP-DMORIE
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in delivery of vector **vaccines**; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT 156287-69-3 161818-44-6, DNA (mouse Flt3 ligand cDNA plus flanks)
162002-36-0 324829-90-5 324829-98-3 324830-52-6 324830-53-7
324830-54-8 324830-55-9
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

IT 155609-51-1 324831-12-1 324831-13-2 324831-15-4 324831-16-5
324831-17-6 324831-18-7 324831-19-8 324831-20-1 324831-21-2
324831-22-3 324831-23-4 324831-24-5 324831-25-6 324831-26-7
324831-27-8 324831-28-9 324831-29-0 324831-30-3 324831-31-4
324831-32-5 324831-33-6 324831-34-7 324831-35-8 324831-36-9
324831-37-0 324831-38-1 324831-39-2
RL: PRP (Properties)
(unclaimed nucleotide sequence; cDNAs encoding the Flt-3 receptor ligand and there use as adjuvants in vector **vaccines**)

L35 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:861431 HCAPLUS
DOCUMENT NUMBER: 134:16550
TITLE: Regulation of systemic immune responses utilizing transgenic cytokines and antigens
INVENTOR(S): Hardy, Steve; Dranoff, Glenn
PATENT ASSIGNEE(S): Cell Genesys, Inc., USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072686	A1	20001207	WO 2000-US15190	20000602

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1999-324707 A 19990602
AB The authors disclose methodol. for stimulating a prophylactic or therapeutic systemic immune response in a mammal to a tumor. Systemic stimulation is achieved by the administration of a tumor cell expressing retrovirally transduced cytokine(s). In one example, B16 melanoma cells were transduced with the MFG vector expressing interleukin-2 (IL-2). Tumor growth was rejected in mice inoculated with live IL-2-expressing B16, however long-term systemic immunity was absent unless the tumor cells were co-transduced for expression of GM-CSF. In a second example, irradiated B16 cells expressing GM-CSF were shown more capable of mediating the rejection of pre-established tumors than were irradiated cells alone and did not exhibit the toxicity of live transduced B16. In addn., addnl. transfection for interferon-.gamma. compromised the ability of the transduced B16 cells to function as an effective vaccine. The authors also disclose recombinant adenovirus encoding granulocyte-macrophage colony stimulating factor,.
IC ICM A01N063-00
ICS A61K048-00; C12N015-00; C12N005-00
CC 15-5 (Immunochemistry)
Section cross-reference(s): 14
IT Animal cell line
(DU-145; stimulation of immune response by **proliferation-incompetent** tumor cell lines transduced for cytokine expression)
IT Animal cell line
(LNCaP; stimulation of immune response by **proliferation-incompetent** tumor cell lines transduced for cytokine expression)
IT Animal cell line
(PC-3; stimulation of immune response by **proliferation-incompetent** tumor cell lines transduced for cytokine expression)
IT Kidney, neoplasm
(carcinoma, inhibitors; **proliferation-incompetent** tumor cells transduced for cytokine expression)
IT Uterus, neoplasm
(cervix, inhibitors; **proliferation-incompetent** tumor cells transduced for cytokine expression)
IT **Antitumor agents**
(cervix; **proliferation-incompetent** tumor cells transduced for cytokine expression)
IT Skin, neoplasm
(epidermis, carcinoma; **proliferation-incompetent** tumor cells transduced for cytokine expression)
IT Ovary, neoplasm
(inhibitors; **proliferation-incompetent** tumor cells transduced for cytokine expression)
IT Gamma ray
(irradn.; of cytokine-transduced tumor cells for induction of **proliferation incompetence**)
IT **Antitumor agents**
(kidney carcinoma; **proliferation-incompetent** tumor cells transduced for cytokine expression)
IT Transduction, genetic

(kit for engineering **GM-CSF** expression in tumor cells)

IT **Antitumor agents**
(leukemia; **proliferation-incompetent** tumor cells transduced for cytokine expression)

IT **Antitumor agents**
(lung non-small-cell carcinoma; **proliferation-incompetent** tumor cells transduced for cytokine expression)

IT **Antitumor agents**
(mammary gland; **proliferation-incompetent** tumor cells transduced for cytokine expression)

IT **Antitumor agents**
(melanoma; **proliferation-incompetent** tumor cells transduced for cytokine expression)

IT **Antitumor agents**
(metastasis; **proliferation-incompetent** tumor cells transduced for cytokine expression)

IT Mammary gland
Prostate gland
(neoplasm, inhibitors; **proliferation-incompetent** tumor cells transduced for cytokine expression)

IT Lung, neoplasm
(non-small-cell carcinoma, inhibitors; **proliferation-incompetent** tumor cells transduced for cytokine expression)

IT Immunosuppression
(of immune response to **proliferation-incompetent** tumor cells transduced for expression of **GM-CSF** and interferon-.gamma.)

IT **Antitumor agents**
(ovary; **proliferation-incompetent** tumor cells transduced for cytokine expression)

IT Intestine, neoplasm
(polyp; **proliferation-incompetent** tumor cells transduced for cytokine expression)

IT Immunostimulants
(**proliferation-incompetent** tumor cells transduced for expression of cytokines)

IT **Antitumor agents**
(**prostate** gland; **proliferation-incompetent** tumor cells transduced for cytokine expression)

IT Cytokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stimulation of immune response by **proliferation-incompetent** tumor cells transduced for cytokine expression)

IT Interleukin 2
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stimulation of immune response by **proliferation-incompetent** tumor cells transduced for expression of)

IT **Antigens**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**; stimulation of immune response by **proliferation-incompetent** tumor cells transduced for expression of)

IT **Vaccines**
(tumor; **proliferation-incompetent** tumor cells

transduced for expression of cytokines)
IT **Antitumor agents**
(**vaccines; proliferation-incompetent** tumor cells transduced for expression of cytokines)
IT **83869-56-1, GM-CSF**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stimulation of immune response by **proliferation-incompetent** tumor cells transduced for expression of)
REFERENCE COUNT: 10
REFERENCE(S):
(1) Chiorini; US 5693531 A 1997 HCAPLUS
(2) Dranoff; US 5637483 A 1997 HCAPLUS
(3) Dranoff; US 5904920 A 1999 HCAPLUS
(4) Drayer, J; Developmental Hematology and Immunology 1997, V32, P131 HCAPLUS
(6) Low; US 5837231 A 1998 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:725747 HCAPLUS
DOCUMENT NUMBER: 133:280559
TITLE: Modified dendritic cells selectin expression and uses in tumor **vaccine**
INVENTOR(S): Kupper, Thomas S.; Robert, Caroline; Von Andrian, Ulrich
PATENT ASSIGNEE(S): The Brigham and Women's Hospital, Inc., USA; The Center for Blood Research, Inc.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000060055	A1	20001012	WO 2000-US8654	20000331

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: US 1999-127423 P 19990401
AB The invention provides isolated dendritic cells genetically modified to express a selectin polypeptide, optionally treated with activated platelets or membrane microparticles thereof. The invention also provides isolated platelet modified dendritic cells. Methods for delivering the modified dendritic cells to peripheral lymph nodes and methods for using the modified dendritic cells to stimulate immune responses also are provided. Vaccine compns. contg. the modified dendritic cells also are provided.
IC ICM C12N005-10
ICS A61K048-00; A61K039-00; A61P035-00
CC 15-2 (Immunochemistry)
Section cross-reference(s): 3, 14
ST recombinant dendritic cell selectin expression lymph node immune stimulation; antitumor **vaccine** recombinant dendritic cell

IT Selectins
RL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(E-, chimera E/L selectin; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Selectins
RL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(L-, chimera E/L selectin; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Selectins
RL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(P-; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Immunostimulants
(adjuvants, in **vaccine** compn. selected from IL-10, TGF-.beta., IL-4, interferon-.gamma., IL-12, GM-CFS, CD40, CD80, and CD86; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Gene, animal
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(antigen encoding, transfection of dendritic cells; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Ras proteins
TCR (T cell receptors)
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(antigen; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(from B cell tumors, antigens; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Immunotherapy
T cell (lymphocyte)
(modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT CD34 (antigen)
CD40 (antigen)
CD80 (antigen)
CD86 (antigen)
Carcinoembryonic antigen
Interleukin 10
Interleukin 12
Interleukin 4
Prostate-specific antigen
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Transformation, genetic
(of dendritic cells; modified dendritic cells selectin expression and uses in tumor **vaccine**)

IT Animal tissue culture
(of isolated dendritic cells; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Lymph node
(peripheral; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Virus vectors
(retrovirus, lentivirus, adenovirus, .lambda. phage; modified dendritic
cells selectin expression and uses in tumor **vaccine**)
IT Appendix
Tonsil
(secondary lymph node; modified dendritic cells selectin expression and
uses in tumor **vaccine**)
IT Ligands
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(selectin (addressins), binding by dentritic cells; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Cell membrane
(selectin ligand expression on , microparticles selectin contg., treatment of transfected dendritic cells; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Gene, animal
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(selectin, transfer of; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Immunity
(to an antigen; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Dendritic cell
(transgenic, expressing human selectin; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Platelet (blood)
(treatment of transfected dendritic cells; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT **Vaccines**
(tumor, therapeutic efficacy of dendritic cells; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT **Antigens**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**tumor-assocd.**, MAGE, MART, LAGE, NY-ESO-1, tyrosinase, PRAME,; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT **Antitumor agents**
(**vaccines**, therapeutic efficacy of dendritic cells; modified dendritic cells selectin expression and uses in tumor **vaccine**
)
IT Murine leukemia virus
(vector, human L-selectin expressing, transformation of dendritic cells
with; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Coliphage .lambda.
Human adenovirus
Lentivirus

Retroviridae
(vector; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Vein
(venule, endothelium; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(.beta.-; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT Interferons
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(.gamma.; modified dendritic cells selectin expression and uses in tumor **vaccine**)
IT **83869-56-1**, Colony-stimulating factor 2
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(expression by tumor cells for induction of antitumor immune response; modified dendritic cells selectin expression and uses in tumor **vaccine**)

REFERENCE COUNT: 7
REFERENCE(S):
(1) Diacovo, T; 39th Annual Meeting of the American Society of Hematology 1997
(2) Diacovo, T; BLOOD, PART 1 1997, V90(10 SUPPL 1), P567A
(3) Kan, M; WO 9846083 A 1998 HCAPLUS
(4) Klein, C; BLOOD, PART 1 1999, V94(10 SUPPL 1), P398
(5) Klein, C; Forty-first Annual Meeting of the American Society of Hematology 1999
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:383976 HCAPLUS
DOCUMENT NUMBER: 133:29611
TITLE: Stimulation of T cells against self antigens using CTLA-4 blocking agents
INVENTOR(S): Allison, James P.; Hurwitz, Arthur A.; Vanelsas, Andrea
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032231	A1	20000608	WO 1999-US28739	19991203

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,

SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-110761 P 19981203

AB Stimulation of T cells to respond to self antigens is achieved through a blockade of CTLA-4 signaling. CTLA-4 blocking agents (e.g. antibody or monoclonal antibody) are combined with antigen prepns., either alone or with addnl. immune response stimulating agents, in costimulation strategies to break immune tolerance and stimulate an enhanced T-cell response against self antigens. This enhanced response is useful for the treatment of non-immunogenic and poorly-immunogenic tumors, as well as other medical conditions requiring selective tissue ablation.

IC ICM A61K039-395
ICS A61K039-00; A61K048-00; C07K014-53; A61K039-395; A61K039-00

CC 15-3 (Immunochemistry)
Section cross-reference(s): 3

ST monoclonal antibody CTLA4 self antigen tumor; cancer **vaccine** CTLA4 blocking agent adjuvant

IT Antibodies
Prostate-specific antigen
neu (receptor)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal anti-CTLA-4 antibody for breaking immune tolerance and for stimulating immune response to non-immunogenic tumor)

IT **Prostate** gland
(neoplasm; monoclonal anti-CTLA-4 antibody for breaking immune tolerance and for stimulating immune response to non-immunogenic tumor)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**prostate** stem cell; monoclonal anti-CTLA-4 antibody for breaking immune tolerance and for stimulating immune response to non-immunogenic tumor)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, **prostate**-specific membrane **antigen**; monoclonal anti-CTLA-4 antibody for breaking immune tolerance and for stimulating immune response to non-immunogenic tumor)

IT **Vaccines**
(tumor; monoclonal anti-CTLA-4 antibody for breaking immune tolerance and for stimulating immune response to non-immunogenic tumor)

IT **Antitumor agents**
(**vaccines**; monoclonal anti-CTLA-4 antibody for breaking immune tolerance and for stimulating immune response to non-immunogenic tumor)

IT **83869-56-1P, GM-CSF**
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal anti-CTLA-4 antibody for breaking immune tolerance and for stimulating immune response to non-immunogenic tumor)

REFERENCE COUNT: 7
REFERENCE(S): (1) Brigham And Women'S Hospital Inc; WO 9842752 A 1998 HCAPLUS

(2) Cepero, E; BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS 1998, V247(3), P838 HCAPLUS
(3) Hurwitz, A; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE U S A 1998, V95(17), P10067 HCAPLUS
(4) Regents Of The University Of California; WO 9720574 A 1997 HCAPLUS
(5) The Regents Of The University Of Michigan; WO 9005541 A 1990 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:314929 HCAPLUS
DOCUMENT NUMBER: 132:333386
TITLE: Cancer-associated antigens and methods of their identification
INVENTOR(S): Ando, Dale; Chang, Ju-Fay; Mcarthur, James; Roberts, Margo; Simons, Jonathon
PATENT ASSIGNEE(S): Cell Genesys, Inc., USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000026676	A1	20000511	WO 1999-US25936	19991103

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-106795 P 19981103
AB The present invention provides novel, isolated, tumor-assocd. antigens, and methods for identifying such antigens in a biol. sample, and of screening for the presence of such an antigen in a biol. specimen, wherein the tumor antigen identified reacts with serum from a subject treated with a vaccine comprising a cytokine and **proliferation-incompetent** tumor cells which express the tumor-assocd. antigen. Also provided are kits for carrying out the methods of the invention.
IC ICM G01N033-68
ICS G01N033-574
CC 15-2 (Immunochemistry)
Section cross-reference(s): 3, 9, 63
ST **tumor assocd antigen** cytokine cancer **vaccine**
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**105**,000-**mol.-wt.**, **tumor-**

assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(12,000-mol.-wt., tumor-
assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(130,000-mol.-wt., tumor-
assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(14,000-mol.-wt., tumor-
assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(150,000-mol.-wt., tumor-
assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(160,000-mol.-wt., tumor-
assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(250,000 mol. wt. tumor-
assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(26,000-mol.-wt., tumor-
assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(27,000-mol.-wt., tumor-
assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(31,000-mol.-wt., tumor-
assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(32,000-mol.-wt., tumor-
assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(60,000-mol.-wt., tumor-
assocd. antigen; tumor-assocd.
antigens and cytokines for diagnosis and therapy of cancer)

IT Polyacrylamide gel electrophoresis
(SDS-; **tumor-assocd. antigens** and
cytokines for diagnosis and therapy of cancer)
IT Immunostimulants
(adjuvants; **tumor-assocd. antigens** and
cytokines for diagnosis and therapy of cancer)
IT Animal tissue
(biopsy; **tumor-assocd. antigens** and
cytokines for diagnosis and therapy of cancer)
IT Diagnosis
(cancer; **tumor-assocd. antigens** and
cytokines for diagnosis and therapy of cancer)
IT Lung, neoplasm
Mammary gland
Prostate gland
(carcinoma; **tumor-assocd. antigens** and
cytokines for diagnosis and therapy of cancer)
IT Intestine, neoplasm
(colon, carcinoma; **tumor-assocd. antigens**
and cytokines for diagnosis and therapy of cancer)
IT Intestine, neoplasm
(colon; **tumor-assocd. antigens** and
cytokines for diagnosis and therapy of cancer)
IT Neoplasm
(diagnosis; **tumor-assocd. antigens** and
cytokines for diagnosis and therapy of cancer)
IT Neoplasm
(hematol.; **tumor-assocd. antigens** and
cytokines for diagnosis and therapy of cancer)
IT Test kits
(immunodiagnostic; **tumor-assocd. antigens**
and cytokines for diagnosis and therapy of cancer)
IT Drug delivery systems
(injections, i.m.; **tumor-assocd. antigens**
and cytokines for diagnosis and therapy of cancer)
IT Drug delivery systems
(injections, intradermal; **tumor-assocd.**
antigens and cytokines for diagnosis and therapy of cancer)
IT Drug delivery systems
(injections, s.c.; **tumor-assocd. antigens**
and cytokines for diagnosis and therapy of cancer)
IT Dyes
(label; **tumor-assocd. antigens** and
cytokines for diagnosis and therapy of cancer)
IT Enzymes, biological studies
Radionuclides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(label; **tumor-assocd. antigens** and
cytokines for diagnosis and therapy of cancer)
IT Drug delivery systems
(liposomes; **tumor-assocd. antigens** and
cytokines for diagnosis and therapy of cancer)
IT Neoplasm
(metastasis, **vaccine; tumor-assocd.**
antigens and cytokines for diagnosis and therapy of cancer)
IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(monoclonal; **tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)
IT Mammary gland
Prostate gland
(neoplasm; **tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)
IT Neoplasm
(**proliferation-incompetent** cells; **tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)
IT Lacrimal gland
Vagina
(secretions; **tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)
IT Plastics, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(support; **tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)
IT **Antitumor agents**
Ascitic fluid
Blood analysis
Blood serum
Carcinoma
Cerebrospinal fluid
Epitopes
Feces
Labels
Leukemia
Lung, neoplasm
Ovary, neoplasm
Saliva
Semen
Urine analysis
Virus vectors
(**tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)
IT DNA
Nucleic acids
RNA
cDNA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)
IT Antibodies
CD2 (**antigen**)
CD80 (**antigen**)
Cell adhesion molecules
Cytokines
Interleukin 1
Interleukin 10
Interleukin **12**
Interleukin 15
Interleukin 18
Interleukin 3
Interleukin 4

Interleukin 6
Interleukin 7
Macrophage inflammatory protein 1.alpha.
Macrophage inflammatory protein 1.beta.
Macrophage inflammatory protein 2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.; tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)

IT Animal cell line
Vaccines
(tumor; **tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)

IT **Antitumor agents**
(**vaccines; tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)

IT Adeno-associated virus
Human adenovirus
Human herpesvirus
Lentivirus
Poxviridae
Retroviridae
Simian virus 40
Sindbis virus
Vaccinia virus
(vector; **tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)

IT Transforming growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-; **tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)

IT **81627-83-0**, M-CSF **83869-56-1**, **GM-CSF**
143011-72-7, G-CSF
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd. antigens** and cytokines for diagnosis and therapy of cancer)

REFERENCE COUNT: 4
REFERENCE(S):
(1) Dranoff, G; US 5637483 A 1997 HCAPLUS
(2) Hersey, P; INT J CANCER 1990, V46, P612 MEDLINE
(3) Simons, J; CANCER RESEARCH 1999, V59, P5160 HCAPLUS
(4) Soiffer, R; PROC NATL ACAD SCI USA 1998, V95, P13141 HCAPLUS

L35 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:241487 HCAPLUS
DOCUMENT NUMBER: 132:289609
TITLE: Sequences encoding novel cancer-associated antigens, and diagnostic/therapeutic uses thereof
INVENTOR(S): Obata, Yuichi; Gout, Ivan; Tureci, Ozlem; Sahin, Ugar;
Pfreundschuh, Michael; Scanlan, Matthew J.; Stockert, Elisabeth; Chen, Yao-tseng; Old, Lloyd J.; Jager, Elke; Knuth, Alex

PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020587	A2	20000413	WO 1999-US22873	19991004
WO 2000020587	A3	20001012		
W: AU, CA, CN, JP, KR, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9965055	A1	20000426	AU 1999-65055	19991004
EP 1117791	A2	20010725	EP 1999-953017	19991004
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-166300 A 19981005
US 1998-166350 A 19981005
WO 1999-US22873 W 19991004

AB Cancer assocd. antigens have been identified by autologous antibody screening of libraries of nucleic acids expressed in renal cancer cells using antisera from cancer patients. The invention relates to nucleic acids and encoded polypeptides which are cancer assocd. antigens expressed in patients afflicted with renal cancer. The invention provides, inter alia, isolated nucleic acid mols., expression vectors contg. those mols. and host cells transfected with those mols. The invention also provides isolated proteins and peptides, antibodies to those proteins and peptides and cytotoxic T lymphocytes which recognize the proteins and peptides. Fragments of the foregoing including functional fragments and variants also are provided. Kits contg. the foregoing mols. addnl. are provided. The mols. provided by the invention can be used in the diagnosis, monitoring, research, or treatment of conditions characterized by the expression of one or more cancer assocd. antigens.

IC ICM C12N015-12
ICS C07K014-47; A61K031-70; A61K035-12; A61K038-13; C07K016-18; G01N033-574; C12Q001-68

CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 1, 6, 14, 15

IT Mammary gland
Prostate gland
(neoplasm, antigens assocd. with; sequences encoding novel cancer-assocd. antigens, and diagnostic/therapeutic uses thereof)

IT **Antitumor agents**
Immunoassay
Molecular cloning
Protein sequences
cDNA sequences
(sequences encoding novel cancer-assocd. antigens, and diagnostic/therapeutic uses thereof)

IT **Antigens**
RL: ANT (Analyte); ANST (Analytical study)
(**tumor-assocd.**, complexed with HLA mol.; sequences encoding novel cancer-assocd. **antigens**, and

diagnostic/therapeutic uses thereof)

IT **Antigens**
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, complexed with a toxin; sequences encoding novel cancer-assocd. **antigens**, and diagnostic/therapeutic uses thereof)

IT **Antigens**
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(**tumor-assocd.**; sequences encoding novel cancer-assocd. **antigens**, and diagnostic/therapeutic uses thereof)

IT **Vaccines**
(tumor; sequences encoding novel cancer-assocd. antigens, and diagnostic/therapeutic uses thereof)

IT Interleukins
Saponins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use as an adjuvant in a **vaccine**; sequences encoding novel cancer-assocd. antigens, and diagnostic/therapeutic uses thereof)

IT **Antitumor agents**
(**vaccines**; sequences encoding novel cancer-assocd. antigens, and diagnostic/therapeutic uses thereof)

IT **83869-56-1, GM-csf**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use as an adjuvant in a **vaccine**; sequences encoding novel cancer-assocd. antigens, and diagnostic/therapeutic uses thereof)

L35 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:240985 HCAPLUS
DOCUMENT NUMBER: 132:292701
TITLE: Novel methods for therapeutic vaccination
INVENTOR(S): Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious; Haaning, Jesper; Leach, Dana; Dalum, Iben; Gautam, Anand; Birk, Peter; Karlsson, Gunilla
PATENT ASSIGNEE(S): M Amp E Biotech A/s, Den.
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020027	A2	20000413	WO 1999-DK525	19991005
WO 2000020027	A3	20001012		

W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,

DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9958510 A1 20000426 AU 1999-58510 19991005
EP 1117421 A2 20010725 EP 1999-945967 19991005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: DK 1998-1261 A 19981005
US 1998-105011 P 19981020
WO 1999-DK525 W 19991005

AB A method is disclosed for inducing cell-mediated immunity against cellular antigens. More specifically, the invention provides for a method for inducing cytotoxic T-lymphocyte immunity against weak antigens, notably self-proteins. The method entails that antigen presenting cells are induced to present at least one CTL epitope of the weak antigen and at the same time presenting at least one foreign T-helper lymphocyte epitope. In a preferred embodiment, the antigen is a cancer specific antigen, e.g. prostate specific membrane antigen (PSM), Her2, or FGF8b. The method can be exercised by using traditional polypeptide vaccination, but also by using live attenuated vaccines or nucleic acid vaccination. The invention furthermore provides immunogenic analogs of PSM, Her2 and FGF8b, as well as nucleic acid mols. encoding these analogs. Also vectors and transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogs of weak or non-immunogenic antigens.

IC A61K039-00

CC 15-2 (Immunochemistry)
Section cross-reference(s): 3, 63

ST weak antigen **vaccine** cytotoxic T lymphocyte; tumor antigen T cell epitope **vaccine**

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(17-1A; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AM-1; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(APC; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(APRIL; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAGE; weak antigens inserted with foreign T cell epitope as

vaccines)
IT Chemokines
(C-X-C, Ena78; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT CD antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD33; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycoproteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD40-L (antigen CD40 ligand); weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD52; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CDC27; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CO17-1A; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CS (circumsporozoite), epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DCC (deleted in colorectal cancer); weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DcR3; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E6; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Transcription factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E7; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Hematopoietin receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FLT3 receptors; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycoproteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(GP1; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(H-ras; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HMTV; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Heat-shock proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HSP 70; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Heat-shock proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HSP 90; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgE type II; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(K-ras; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Lipoprotein receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LDL, fusion with FUT or fucosyltransferase; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MCP (membrane cofactor protein); weak antigens inserted with foreign T
cell epitope as **vaccines**)
IT Multidrug resistance proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MDR1; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MHC (major histocompatibility complex), class I; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MHC (major histocompatibility complex), class II; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Diglycerides
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-acyl; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-ras; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Glycoproteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(P170; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Phosphoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(P210bcr-c-abl; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT **Prostate**-specific antigen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PSA and PSM; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Hemopoietins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Progenipoietin; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Transcription factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Rb; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SART-1; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Gene, animal
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SSX; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Transcription factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STAT3; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Mucins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STn antigen; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TAG-72 (**tumor-assocd.** glycoprotein 72); weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TPA (tissue protein antigen); weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TRP-1 (tyrosinase-related protein 1); weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TRP-2 (tyrosinase-related protein 2); weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Immunostimulants
(adjuvants, Freund's incomplete; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Immunostimulants
(adjuvants, Freund's; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Immunostimulants
(adjuvants, ISCOMs; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Immunostimulants
(adjuvants, Ribi; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Immunostimulants
(adjuvants; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(anal; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Animal virus
Bacteria (Eubacteria)
Parasite
(antigen; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bcl-2; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(buccal; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Transcription factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-myc; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Diagnosis
(cancer; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT T cell (lymphocyte)
(cytotoxic, epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Mutation
(deletion; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Neoplasm
(diagnosis; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Toxoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria, epitope; weak antigens inserted with foreign T cell

epitope as **vaccines**)
IT Glycophosphoproteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(endoplasmins; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enterotoxins, heat-labile; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(epidural; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Mucins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(episialins; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT B cell (lymphocyte)
T cell (lymphocyte)
(epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Hemagglutinins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Functional groups
(farnesyl; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(folate; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene KDR; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Functional groups
(geranyl-geranyl; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Protein motifs
(glycosylation site; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycoproteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gp100; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycoproteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gp15; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Sialoglycoproteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gp75; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT T cell (lymphocyte)
(helper cell, epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Phosphoproteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hsc 70 (heat-shock cognate, 70,000-**mol.**-**wt.**); weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(injections, s.c.; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Mutation
(insertion; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Interleukin receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interleukin 13 receptors; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(intracranial; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(intracutaneous; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(intradermal; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Hemolysins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(listeriolysins; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mammaglobin; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanoma-assocd., MAGE; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanoma-assocd., Melan-A/MART-1; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Transferrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanotransferrins; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Chromosome
(minichromosomes; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Chemicals
(modification; weak antigens inserted with foreign T cell epitope as

vaccines)
IT Mucins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mucin 2, 3 and 4; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Functional groups
(myristyl; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT DNA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(naked; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Mammary gland
Prostate gland
(neoplasm; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Microorganism
(non-pathogenic; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Liquids
(oils formulation; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(oral; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p15; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Functional groups
(palmitoyl; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(parenterals; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Drug delivery systems
(peritoneal; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycolipoproteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphatidylinositol-contg.; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(probasins; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**prostateins**; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Interleukin 13
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(receptors; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Proteins, specific or class

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(self; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Drug delivery systems
(spinal; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Drug delivery systems
(subdermal; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Drug delivery systems
(sublingual; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Mutation
(substitution; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surface; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(terminator; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Toxoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tetanus, epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transfection-facilitating; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transmembrane, mesothelin; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, G250; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, GAGE; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, KIAA0205 bladder carcinoma **antigen**; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, MAP17; weak **antigens** inserted with foreign T cell epitope as **vaccines**)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, MIC A/B; weak **antigens**

inserted with foreign T cell epitope as **vaccines**)
IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, MUM-1; weak **antigens**
inserted with foreign T cell epitope as **vaccines**)
IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, NY-ESO-1; weak **antigens**
inserted with foreign T cell epitope as **vaccines**)
IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, PRAME; weak **antigens**
inserted with foreign T cell epitope as **vaccines**)
IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, Pmel-17; weak **antigens**
inserted with foreign T cell epitope as **vaccines**)
IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, RCAS1; weak **antigens**
inserted with foreign T cell epitope as **vaccines**)
IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, ZAG; weak **antigens**
inserted with foreign T cell epitope as **vaccines**)
IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**, p16INK4; weak **antigens**
inserted with foreign T cell epitope as **vaccines**)
IT **Antigens**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**; weak **antigens** inserted
with foreign T cell epitope as **vaccines**)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor-rejection, RAGE-1; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Complement receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type 1; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Complement receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type 2; weak antigens inserted with foreign T cell epitope as **vaccines**)
IT Animal
Animal cell line
Antigen-presenting cell
Antitumor agents
Bacteriophage
Carriers
Cosmids
DNA sequences
Dendritic cell

Encapsulation
Epitopes
Immunotherapy
Influenza virus
Latex
Liposomes
Macrophage
Micelles
Molecular cloning
Mycobacterium
Particles
Plasmids
Plasmodium falciparum
Protein sequences
Quillaja saponaria
Vaccines
Virus
Virus vectors
(weak antigens inserted with foreign T cell epitope as **vaccines**
)

IT Gene, animal
Promoter (genetic element)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(weak antigens inserted with foreign T cell epitope as **vaccines**
)

IT CA 125 (carbohydrate antigen)
CD19 (antigen)
CD20 (antigen)
CD22 (antigen)
CD44 (antigen)
CD45 (antigen)
CD5 (antigen)
CD59 (antigen)
Carcinoembryonic antigen
Enzymes, biological studies
Epidermal growth factor receptors
Haptens
.alpha.-Fetoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(weak antigens inserted with foreign T cell epitope as **vaccines**
)

IT Antibodies
Antigens
CD40 (antigen)
CTLA-4 (antigen)
Calreticulin
Carbohydrates, biological studies
Cytokines
DNA
Heat-shock proteins
Insulin-like growth factor I receptors
Interleukin 1
Interleukin **12**
Interleukin 13
Interleukin 15
Interleukin 2

Interleukin 4
Interleukin 6
Ki-67 antigen
Lipid A
Lipids, biological studies
Osteonectin
Plastics, biological studies
Platelet-derived growth factors
Polymers, biological studies
Receptors
Saponins
Toxins
Tumor necrosis factors
neu (receptor)
p53 (protein)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(weak antigens inserted with foreign T cell epitope as **vaccines**
)

IT Transforming growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.-; weak antigens inserted with foreign T cell epitope as
vaccines)

IT Catenins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-; weak antigens inserted with foreign T cell epitope as
vaccines)

IT Transforming growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-; weak antigens inserted with foreign T cell epitope as
vaccines)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.; weak antigens inserted with foreign T cell epitope as
vaccines)

IT 39391-18-9
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2; weak antigens inserted with foreign T cell epitope as
vaccines)

IT 62031-54-3, FGF
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(8a and 8b isoforms; weak antigens inserted with foreign T cell epitope
as **vaccines**)

IT 264178-47-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(P2 epitope gene; weak antigens inserted with foreign T cell epitope as
vaccines)

IT 126779-13-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(P2 epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 264185-70-8P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(P30 epitope gene; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 126779-14-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(P30 epitope; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 99-20-7D, Trehalose, diester 7429-90-5, Aluminum, biological studies 9004-54-0, Dextran, biological studies 9005-25-8, Starch, biological studies 25322-68-3 53678-77-6, Muramyl dipeptide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 148997-75-5, Androgen-induced growth factor (mouse clone pSC17 precursor reduced) 264179-58-0 264179-59-1, Neu (receptor) (human) 264179-62-6 264179-64-8 264179-65-9 264179-66-0 264179-67-1 264179-68-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 3458-28-4, Mannose 9036-88-8, Mannan
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding partner; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 56093-23-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion with LDL receptor; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 125978-95-2, Nitric oxide synthase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inducible; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 9030-23-3, Thymidine phosphorylase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 141907-41-7, Matrix metalloproteinase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isoforms; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 100040-73-1, DNA (human clone .lambda.HER2-436 gene HER2 receptor cDNA) 264179-57-9 264179-60-4 264179-61-5 264179-63-7
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 52-90-4, Cysteine, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(residue; weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 264134-70-5P 264134-71-6P 264134-72-7P 264134-73-8P 264134-78-3P 264224-61-5P 264224-76-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 71965-46-3, Cathepsins 99085-47-9, Complement decay-accelerating factor 147014-97-9, Cyclin-dependent kinase 4 179241-78-2, Caspase 8
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 251541-10-3, Human Her2 protein (59-73) 251542-12-8, Human Her2 protein (465-479) 264617-99-4, Human PSM (87-108) 264618-03-3, Human PSM (210-230) 264618-06-6, Human PSM (269-289) 264618-07-7, Human PSM (298-324) 264618-08-8, Human PSM (442-465) 264618-09-9, Human PSM (488-514) 264618-23-7, Human PSM (598-630) 264619-18-3, Human PSM (643-662) 264619-84-3, Human PSM (672-699) 264620-57-7, Human Her2 protein (5-25) 264620-84-0, Human Her2 protein (103-117) 264621-04-7, Human Her2 protein (149-163) 264621-94-5, Human Her2 protein (210-224) 264622-06-2, Human Her2 protein (**250**-264) 264622-08-4, Human Her2 protein (325-339) 264622-09-5, Human Her2 protein (369-383) 264622-23-3, Human Her2 protein (579-593) 264624-69-3, Human Her2 protein (632-652) 264624-79-5, Human Her2 protein (653-667) 264624-80-8, Human Her2 protein (661-675) 264625-23-2, Human Her2 protein (695-709) 264625-25-4, Human Her2 protein (72-86) 264625-36-7,
Human Her2 protein (146-**160**) 264625-37-8, Human Her2 protein (221-235) 264625-38-9, Human Her2 protein (257-271) 264625-51-6, Human
FGF8b protein (1-54) 264626-02-0, Human FGF8b protein (55-58) 264626-17-7, Human FGF8b protein (178-215) 264626-69-9, Human FGF8b protein (63-68) 264626-82-6, Human FGF8b protein (72-76) 264626-84-8, Human FGF8b protein (85-91) 264626-85-9, Human FGF8b protein (95-102) 264626-86-0, Human FGF8b protein (106-111) 264626-87-1, Human FGF8b protein (115-120) 264627-05-6, Human FGF8b protein (128-134) 264627-07-8, Human FGF8b protein (138-144) 264627-09-0, Human FGF8b protein (149-154) 264627-10-3, Human FGF8b protein (158-162) 264627-11-4, Human FGF8b protein (173-177) 264627-12-5, Human FGF8b protein (**26**-45)
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(weak antigens inserted with foreign T cell epitope as **vaccines**)

IT 3700-67-2 9001-91-6, Plasminogen 9002-10-2, Tyrosinase 9002-61-3, Human chorionic gonadotropin 9032-22-8, Mox1 oxidase 9034-40-6, Gonadotropin-releasing hormone 9081-34-9, 5.alpha. Reductase 50812-37-8, Glutathione S-transferase 60748-06-3, Gastrin 17 62010-37-1, GD3 65988-71-8, GD2 66456-69-7, GM4 66594-14-7, Quil A 80043-53-4, Gastrin-releasing peptide 83588-90-3, N-Acetylglucosaminyltransferase V **83869-56-1**, **GM-CSF** 89800-66-8, Heparanase 120178-12-3, Telomerase

127464-60-2, Vascular endothelial growth factor 140208-23-7, Plasminogen
activator inhibitor-1 141256-04-4, QS21
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(weak antigens inserted with foreign T cell epitope as **vaccines**
)
IT 61512-21-8, Thymosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta. 15; weak antigens inserted with foreign T cell epitope as
vaccines)
IT 9005-80-5, Inulin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.-; weak antigens inserted with foreign T cell epitope as
vaccines)

L35 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:220702 HCAPLUS
DOCUMENT NUMBER: 132:250003
TITLE: Enhanced immune response to **tumor-assocd. antigens** by recombinant virus expressing an immunostimulatory molecule
INVENTOR(S): Schlom, Jeffrey; Kantor, Judith; Hodge, James W.
PATENT ASSIGNEE(S): United States of America, Department of Health and Human Services, USA
SOURCE: U.S., 35 pp., Cont.-in-part of U.S. Ser. No. 317,268, abandoned.
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WO 9610419	A2	19960411	WO 1995-US12624	19951002
WO 9610419	A3	19960517		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9537353	A1	19960426	AU 1995-37353	19951002
AU 688606	B2	19980312		
EP 784483	A2	19970723	EP 1995-935264	19951002
EP 784483	B1	20001129		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10506902	T2	19980707	JP 1995-512100	19951002
EP 1016418	A2	20000705	EP 2000-102998	19951002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
AT 197765	E	20001215	AT 1995-935264	19951002
ES 2154738	T3	20010416	ES 1995-935264	19951002

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AB The authors disclose the prepn. and immunol. activity of recombinant viral vectors into which exogenous tumor-assocd. antigens and costimulatory mols. were engineered. In one example, mice were prophylactically immunized with vaccinia viruses expressing carcinoembryonic antigen and B7 antigens. Immunized animals developed a cellular response against CEA and were free from tumor development on challenge with a colon adenocarcinoma cell line. In a second example, mice immunized with vectors expressing prostate-specific antigen and B7 costimulatory mol. were shown to develop a cytotoxic T-cell response to PSA that exceeded that obsd. on immunization with PSA-expressing virus alone.

IC ICM A61K039-00
ICS C12N015-00

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CC 15-2 (Immunochemistry)
Section cross-reference(s): 1

ST tumor antigen **vaccine** virus vector costimulatory mol

IT CD **antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD72; as costimulatory mol. for viral vectors inducing enhanced immune response against **tumor-assocd. antigens**)

IT **Antitumor agents**
(Hodgkin's disease inhibitors; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT Cell adhesion molecules
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ICAM-1 (intercellular adhesion mol. 1); as costimulatory mol. for viral vectors inducing enhanced immune response against **tumor-assocd. antigens**)

IT Mucins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Muc-2; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TAG-72 (**tumor-assocd.** glycoprotein 72); enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT **Prostate** gland
(adenocarcinoma, inhibitors; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT **Antitumor agents**
(adenocarcinoma; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT CD80 (**antigen**)
CD86 (**antigen**)
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(as costimulatory mol. for viral vectors inducing enhanced immune response against **tumor-assocd. antigens**)

IT Interleukin 12
Interleukin 2
Interleukin 6
LFA-3 (**antigen**)
Tumor necrosis factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as costimulatory mol. for viral vectors inducing enhanced immune response against **tumor-assocd. antigens**)

IT Adenoviridae
Canarypox virus
Fowlpox virus
Human poliovirus
Retroviridae
Swinepox virus
Vaccinia virus
(as vector for **tumor-assocd. antigen** and immunostimulatory mols.)

IT **Antitumor agents**
(colon adenocarcinoma; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT Intestine, neoplasm
(colon, adenocarcinoma, inhibitors; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT Virus vectors
(enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT Carcinoembryonic **antigen**
Prostate-specific **antigen**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT CA 125 (carbohydrate **antigen**)
Ras proteins
neu (receptor)
p53 (protein)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT Mucins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(episialins; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT Liver, neoplasm
(hepatoma, inhibitors; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT **Antitumor agents**
(hepatoma; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT Growth factor receptors

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heregulin, erbB-3; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT Hodgkin's disease
Lung, neoplasm
(inhibitors; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT **Antitumor agents**
(leukemia; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT **Antitumor agents**
(lung; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanoma-assocd., MAGE-1; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanoma-assocd., MAGE-3; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanoma-assocd., Melan-A/MART-1; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanoma-assocd., gp100; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT **Antitumor agents**
(melanoma; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT **Antitumor agents**
(non-Hodgkin's lymphoma; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oncofetal; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT **Antitumor agents**
(**prostate** adenocarcinoma; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT Heregulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptors, ErbB-3; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)

IT **Antitumor agents**
(sarcoma; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)

IT Thymus gland
(thymoma, inhibitors; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)
IT **Antitumor agents**
(thymoma; viral vectors expressing **tumor-assocd. antigen** and immunostimulatory mols. as)
IT **Antigens**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)
IT **Vaccines**
(tumor; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)
IT **Antitumor agents**
(**vaccines**; enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)
IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.; as costimulatory mol. for viral vectors inducing enhanced immune response against **tumor-assocd. antigens**)
IT **83869-56-1, GM-CSF**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as costimulatory mol. for viral vectors inducing enhanced immune response against **tumor-assocd. antigens**)
IT 9002-10-2, Tyrosinase 137632-09-8, c-ErbB-2 tyrosine kinase 147014-95-7, C-ErbB-3 protein kinase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced immune response to **tumor-assocd. antigens** by viral vectors expressing tumor **antigen** and immunostimulatory mols.)
IT 262840-96-0, 1: PN: US6045802 SEQID: 5 unclaimed DNA 262840-97-1, 2: PN:
US6045802 SEQID: 6 unclaimed DNA 262840-98-2, 3: PN: US6045802 SEQID: 7 unclaimed DNA 262840-99-3, 4: PN: US6045802 SEQID: 8 unclaimed DNA 262841-00-9, 5: PN: US6045802 SEQID: 9 unclaimed DNA 262841-01-0, 6: PN:
US6045802 SEQID: 1 unclaimed DNA 262841-02-1, 7: PN: US6045802 SEQID: 2 unclaimed DNA 262841-03-2, 8: PN: US6045802 SEQID: 3 unclaimed DNA 262841-04-3, 9: PN: US6045802 SEQID: 4 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; enhanced immune response to **tumor-assocd. antigens** by recombinant virus expressing an immunostimulatory mol.)

REFERENCE COUNT: 69
REFERENCE(S): (2) Anon; WO 91/02805 1991 HCAPLUS
(3) Anon; WO 92/19266 1992 HCAPLUS
(4) Anon; WO 9220356 1992 HCAPLUS
(5) Anon; WO 94/16716 1994 HCAPLUS
(8) Azuma; Nature 1993, V366, P76 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> fil wpids

FILE 'WPIDS' ENTERED AT 13:20:22 ON 06 AUG 2001
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                DEL HIS Y
L1           343 S  (TUMOR OR TUMOUR) (2W) ASSOC? (4A) ANTIGEN#
L2             5 S  PROLIFERA? (2W) INCOMP?
L3             1 S L1 AND L2
L4         12779 S  VACCINE#
L5             0 S 16/DC
L6        196430 S D16/DC
L7           285 S L6 AND L1
L8            96 S L7 AND L4
L9          3635 S CYTOKINE#
L10          744 S GM CSF OR GRANULOCYTE# MACROPHAGE# COLONY STIMULA? FACTOR#
L11           17 S L7 AND L10
L12           11 S L4 AND L11
L13           21 S L9 AND L8
L14           26 S L13 OR L12
L15        19556 S HIS
L16            4 S L2 AND (L4 OR L10)
L17           29 S L16  OR L3 OR L14

     FILE 'WPIDS' ENTERED AT 13:20:22 ON 06 AUG 2001

=> d .wp 1-29


L17  ANSWER 1 OF 29  WPIDS COPYRIGHT 2001   DERWENT INFORMATION LTD
AN   2001-381489 [40]   WPIDS
DNC  C2001-116869
TI   Compositions for use in a vaccine for treating, e.g., breast,
     lung and colon cancer comprises at least one peptide that comprises an
```

isolated epitope of a **tumor-associated antigen**

.

DC B04 **D16**

IN CELIS, E; CHESNUT, R; FIKES, J; KEOGH, E; SETTE, A; SIDNEY, J; SOUTHWOOD, S

PA (EPIM-N) EPIMMUNE INC

CYC 94

PI WO 2001041741 A1 20010614 (200140)* EN 86p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

ADT WO 2001041741 A1 WO 2000-US34318 20001213

PRAI US 2000-583200 20000530; US 1999-170448 19991213; US 2000-543608 20000405

AB WO 200141741 A UPAB: 20010719

NOVELTY - Composition (I) comprising at least one peptide that comprises an isolated, prepared epitope consisting of a sequence selected from 25 fully defined short amino acid sequences (S1)-(S25) given in the specification is new.

DETAILED DESCRIPTION - Composition (I) comprises at least one peptide that comprises an isolated, prepared epitope consisting of a sequence selected from:

(i) (S1) VLYGPDAPTV;
(ii) (S2) YLSGANLNV;
(iii) (S3) ATVGIMIGV;
(iv) (S4) LLPENNVLSPV;
(v) (S5) KLCPVQLWV;
(vi) (S6) KLB(sic)PVQLWV;
(vii) (S7) SLPPPGTRV;
(viii) (S8) SMPPPGTRV;
(ix) (S9) KLFGSLAFV;
(x) (S10) KVFGSLAFV;
(xi) (S11) VMAGVGSPYV;
(xii) (S12) ALCRWGLLL;
(xiii) (S13) FLWGPRALV;
(xiv) (S14) HLYQGCQVV;
(xv) (S15) ILHNGAYSL;
(xvi) (S16) IMIGVLVGV;
(xvii) (S17) KIFGSLAFL;
(xviii) (S18) KVAELVHFL;
(xix) (S19) LLTFWNPPV;
(xx) (S20) LVFGIELMEV;
(xxi) (S21) QLVFGIELMEV;
(xxii) (S22) RLLQETELV;
(xxiii) (S23) VVLGVVFGI;
(xxiv) (S24) YLQLVFGIEV; and
(xxv) (S25) YMIMVKCWMI.

INDEPENDENT CLAIMS are also included for the following:

(1) a composition (II) comprising one or more peptides, and further comprising at least two epitopes selected from (S1)-(S25), where each of the one or more peptides comprise less than 50 contiguous amino acids that have 100% identity with a native peptide sequence; and

(2) a vaccine composition (III) comprising an epitope selected from (S1)-(S25) and a pharmaceutical excipient.

ACTIVITY - Cytostatic; immunomodulator.

No supporting data given.

MECHANISM OF ACTION - Vaccine (claimed); immunotherapy.

The peptides of (I) were evaluated for their potential to stimulate cytotoxic T lymphocyte (CTL) precursor responses to the tumor associated antigen (TAA)-derived peptide (in vitro primary CTL induction) and CTL recognition of tumor cells expressing the target TAA peptide epitope (recognition of endogenous targets). These criteria provided evidence that the peptides were functional epitopes.

Peripheral blood monocytic cell-derived (or bone-marrow-derived) human dendritic cells (DC), generated in vitro using granulocyte macrophage-colony stimulating factor (GM-CSF) and Interleukin-4 (IL-4) and pulsed with a peptide of interest, were used as antigen presenting cells (APCs) in primary CTL induction cultures. The peptide pulsed DC were incubated with CD8 T cells (positively selected from normal donor lymphocytes using magnetic beads) which served as the source of CTL precursors. One week after stimulation with peptide, primary cultures were tested for epitope-specific CTL activity using either a standard chromium-release assay which measures cytotoxicity or a sandwich ELISA-based interferon gamma (IFN gamma) production assay. Each of the CTL epitopes stimulated CTL induction from CD 8 T cells of normal donors.

USE - The peptide epitope compositions (I)-(II) are useful for monitoring an immune response to a tumor associated antigen or when one or more peptides are combined to create a vaccine (III) that stimulates the cellular arm of the immune system. In particular, the vaccine mediates immune responses against tumors in individuals who bear an allele of the human leukocyte antigen-A2 supertype (HLA-A2) and improve the standard of care for patients being treated for breast, colon, or lung cancer.

Dwg.0/5

L17 ANSWER 2 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-355609 [37] WPIDS
DNC C2001-110279
TI Enhancing immunogenicity of peptide containing class I epitope, useful for treating cancer, comprises providing (semi-)conservative amino acid substitutions at specified positions of these epitopes.
DC B04 **D16**
IN ISHIOKA, G; SETTE, A; TANGRI, S
PA (EPIM-N) EPIMMUNE INC
CYC 94
PI WO 2001036452 A2 20010525 (200137)* EN 96p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
ADT WO 2001036452 A2 WO 2000-US31856 20001120
PRAI US 2000-239008 20001006; US 1999-166529 19991118
AB WO 200136452 A UPAB: 20010704

NOVELTY - Enhancing (M1) immunogenicity of a peptide comprising a first class I epitope (E) consisting of a sequence having N- and C-terminus (T) and a primary anchor residue (R) comprising introducing (semi) conservative substitution(s) between (T) at position 3, 5 and/or 7 provided the position is not (R), thus making a peptide comprising a second class I epitope with enhanced immunogenicity, is new.

DETAILED DESCRIPTION - M1 comprising providing a peptide containing a first class I epitope where the epitope consists essentially of an amino acid sequence having an N- and a C-terminus and at least one primary anchor residue, where the amino acid residues are numbered consecutively and the primary anchor residue nearest the N-terminus of the epitope is at position 2 or 3, and introducing (semi-)conservative substitution(s) between the N- and the C-terminus of the epitope at position 3, 5 and/or 7 provided the position is not a primary anchor residue, thus constructing a peptide comprising a second class I epitope which exhibits enhanced immunogenicity compared to the first class I epitope, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) a peptide (I) comprising the second class I epitope prepared by M1;

(2) a composition (II) comprising (I);

(3) a nucleic acid molecule (III) comprising a nucleotide sequence encoding a peptide of 9-15 amino acids which contains a second class I epitope obtained by M1; and

(4) a pharmaceutical composition (IV) which comprises (III) as an active ingredient.

ACTIVITY - Cytostatic; antitumor; virucide.

MECHANISM OF ACTION - **Vaccine**; inducer of immune response (claimed). Immunogenicity of analogs for murine p53.261 epitope was tested. To test for immunogenicity in vivo, the human leukocyte antigen (HLA)-A2.1-restricted murine p53.261 epitope was used since cytotoxic T lymphocyte (CTL) responses against this epitope have been shown to be partially tolerized in HLA-A2.1/Kb transgenic mice. Immunogenicity for the p53.261 predicted analogs were tested in HLA-A2.1/Kbxd transgenic mice by co-immunizing mice with 50 micro g of the p53.261 epitope (LLGRDSFEV) or its predicted analogs and 140 micro g of HBV (undefined) core.128 helper epitope in IFA (undefined). Eleven days later, primed spleen cells were harvested and cultured in vitro with irradiated syngeneic LPS (undefined)-activated spleen cells that had been pulsed with 10 micro g/ml of peptide. After 10 days of culture, CTL were restimulated with peptide-pulsed LPS blasts in the presence of Con A-conditioned media as a source of interleukin-2 (IL2). Spleen cells from mice immunized with the predicted analogs were stimulated in vitro against both wild type peptide and the respective immunizing analog. All short-term, bulk populations of CTL were tested for peptide specificity by the interferon gamma (IFN gamma) in situ enzyme linked immunosorbant (ELISA) assay 5 days after the second restimulation in vitro, using Jurkat-A2.1 tumor cells as APC. Alternatively, CTL responses were performed on freshly isolated spleen cells from immunized animals using the Elispot assay. A panel of nine analogs of the p53.261 epitope consisting of three conservative or semi-conservative substitutions at positions 3,5 and 7 of the 9-mer

peptide was tested for immunogenicity in HLA-A2.1/Kbxd transgenic mice. Immunization of mice with each of the nine analogs and in vitro expansion of primed splenocytes with the respective immunizing analog resulted in identification of six analogs (L7, D3, H7, H3, N5, G5) that gave CTL responses characterized by IFN gamma production of 100 pg/well at much lower peptide concentrations compared to CTL induced in vivo and expanded in vitro with wild type peptide. Spleen cells from mice immunized with either wild type (WT) peptide or the indicated analogs were stimulated in vitro with the corresponding immunizing peptide or with WT peptide. IFN gamma release by these CTL's was then measured over a dose range against targets pulsed with the immunizing peptide or with WT peptide. These results indicated that a significant percentage of the analogs induced CTL of a higher avidity than those induced by wild type peptide itself.

USE - (I) is useful for eliciting an immune response by contacting CTLs with (I), where contacting is carried out in vitro in the presence of an antigen presenting cell, or by administering to a subject a nucleic acid molecule comprising a nucleotide sequence encoding (I) (claimed). (I) is useful as reagent to evaluate an immune response and the efficacy of the **vaccine**, and for making antibodies. (I), (II) and (IV) are useful for treating cancer, viral diseases and tumor.

ADVANTAGE - Peptides prepared by (M), contains epitopes which have enhanced ability to affect an immune response with respect to corresponding analogs wild-type epitope.

Dwg.0/12

L17 ANSWER 3 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-343708 [36] WPIDS
DNC C2001-106462
TI Use of antibodies in **vaccines**, for treatment or prevention of tumors, where antibodies are affinity purified from the patient's serum and are directed against anti-tumor antibodies.
DC B04 **D16**
IN ECKERT, H; HIMMLER, G; LOIBNER, H
PA (IGEN-N) IGENEON KREBS IMMUNTHERAPIE FORSCHUNGS
CYC 94
PI WO 2001035989 A2 20010525 (200136)* DE 36p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
ADT WO 2001035989 A2 WO 2000-EP11306 20001115
PRAI AT 1999-1927 19991116
AB WO 200135989 A UPAB: 20010628
NOVELTY - Use of antibodies (Ab) for preparing a **vaccine** (A) for therapeutic or prophylactic immunization against cancer in which Ab are isolated from body fluid by immunoaffinity, using as affinity ligands antibodies (Ab1) that recognize one or more **tumor-associated antigens** (Ag), or their fragments with the same idiotype.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) use of isolated, ex vivo-cultured, dendritic cells (DC) from an

individual for preparation of a **vaccine** (A1), for same use as (A), in which DC have been incubated in vitro with Ab;

(b) pharmaceutical composition containing Ab or the DC of (a); and

(c) preparation of an antibody composition by affinity purification, using Ab1 as the affinity ligand.

ACTIVITY - Antitumor; immunostimulatory. No biodata is provided.

MECHANISM OF ACTION - **Vaccine**.

USE - (A), also (A)-treated dendritic cells, are useful in **vaccines** against tumors, including suppression of new metastases or elimination of residual cells after tumor resection.

ADVANTAGE - (A) are autologous. The method eliminates the need to produce anti-idiotypic antibodies in cultured cells, which is not limited to monoclonal antibodies. The **vaccines** may be subjected to heat treatment to attenuate/inactivate infectious pathogens, eliminating the need for antimicrobial additives; increase immunogenicity of Ab (associated with partial denaturation) and delay release of Ab from the adjuvant (longer-lasting effect).

Dwg.0/6

L17 ANSWER 4 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-328785 [34] WPIDS
DNC C2001-100875
TI Enhancing immune recognition, useful for protecting or treating an individual against malignancies (e.g. leukemia) or infections, by administering modified tumor cells that express interferon consensus sequence binding protein.
DC B04 D16
IN DALEY, G Q; DENG, M
PA (WHED) WHITEHEAD INST BIOMEDICAL RES
CYC 21
PI WO 2001032843 A2 20010510 (200134)* EN 42p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: CA JP
ADT WO 2001032843 A2 WO 2000-US41743 20001101
PRAI US 1999-163167 19991102
AB WO 200132843 A UPAB: 20010620

NOVELTY - Enhancing immune recognition of cells present in an individual and which cause a disease in the individual, comprises introducing into the individual modified cells (referred to as ICSBP-expressing cells) that express interferon consensus sequence binding protein (ICSBP) at a sufficient level to stimulate an immune response to the disease-causing cells in the individual.

DETAILED DESCRIPTION - Enhancing immune recognition of cells present in an individual and which cause a disease in the individual, comprises introducing into the individual modified cells (referred to as ICSBP-expressing cells) that express interferon consensus sequence binding protein (ICSBP) at a sufficient level to stimulate an immune response to the disease-causing cells in the individual. The immune response is greater than the immune response that occurs if ICSBP-expressing cells are not introduced into the individual to enhance immune recognition of the disease-causing cells. INDEPENDENT CLAIMS are also included for the following:

(1) a method of increasing the immunostimulatory effect of a cell comprising enhancing ICSBP expression in the cell;

(2) a tumor cell, referred to as a modified tumor cell, which is replication- or **proliferation-incompetent** and expresses ICSBP encoded by exogenous DNA;

(3) a method of treating a mammal in whom tumor cells are present, comprising co-administering to the mammal at least one chemotherapeutic agent and the modified tumor cells that express ICSBP from exogenous DNA;

(4) an in vitro method of producing tumor-directed cytotoxic T cell clones comprising:

(a) combining T cells obtained from a mammal, appropriate growth factors and target cells that express ICSBP and against which cytotoxic T-cell clones are to be produced, therefore producing a combination; and

(b) maintaining the combination under conditions appropriate for T cell activation and proliferation, therefore producing cytotoxic T-cells clones directed against the target cells;

(5) a method of producing a mammalian cell that expresses ICSBP comprising activating a gene that encodes ICSBP, where the gene is a silent gene that is not normally expressed in the mammalian cell;

(6) a genetically engineered mammalian cell that expresses ICSBP from a normally silent, activated endogenous gene; and

(7) a method of enhancing the ability of an individual to eliminate cells that cause a condition in the individual, comprising increasing ICSBP levels in the individual to a level which results in elimination of the cells to a greater extent than would occur if ICSBP levels were not increased in the individual.

ACTIVITY - Cytostatic; antimicrobial; immunosuppressive.

To test whether ICSBP-induced immunity could eradicate pre-existing disease, 106 Ba-P210 cells were first injected into naive Balb/c mice to induce leukemia. A single dose of 106 Ba-P210-ICSBP cells were injected simultaneously into the same hosts or following a delaying of 3, 7 or 14 days. Simultaneous injection of both cell lines allowed survival of all mice. When leukemia was allowed to develop for 14 days, equivalent to 2 out of 3 of the disease latency, all mice achieved prolonged survival and 20% of the mice survived disease free. These results demonstrated that the anti-leukemic effect of the immunized cells could be initiated rapidly, and that ectopic ICSBP expression in leukemic cells was potent enough to eradicate established disease.

MECHANISM OF ACTION - **Vaccine.**

USE - The ICSBP-expressing cells are useful for protecting or treating an individual against malignancies, infections or autoimmune conditions. In particular, the method is useful for enhancing an individual's ability to eliminate cells that cause a disorder, e.g. tumor cells (e.g. chronic myeloid leukemia cells or solid tumor cells) or cell infected with a pathogen (e.g. a virus, a bacterium, a mycobacterium, a parasite, a yeast or a protozoan).

Dwg.0/6

L17 ANSWER 5 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-290921 [30] WPIDS
DNC C2001-089277
TI New chimeric polypeptide, useful as anti-tumor **vaccines**, comprises carboxy terminal fragment of heat shock protein, Flt-3 ligand or cytoplasmic translocation domain of Pseudomonas exotoxin A and antigenic polypeptide.
DC B04 **D16**

IN HUNG, C; WU, T
PA (UYJO) UNIV JOHNS HOPKINS SCHOOL MEDICINE
CYC 94
PI WO 2001029233 A2 20010426 (200130)* EN 110p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
ADT WO 2001029233 A2 WO 2000-US41422 20001020
PRAI US 2000-501097 20000209; US 1999-421608 19991020
AB WO 200129233 A UPAB: 20010603
NOVELTY - A chimeric polypeptide (I) comprising:
(a) a first polypeptide domain containing a carboxy terminal fragment of a heat shock protein (HSP), an Flt-3 ligand (FL), or a cytoplasmic translocation domain of a Pseudomonas exotoxin A (ETA dII); and
(b) a second polypeptide domain containing an antigenic polypeptide, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a nucleic acid (II) encoding (I) comprising a first polypeptide domain containing a carboxy terminal fragment of a HSP, an FL, an ETA dII or a **granulocyte-macrophage colony stimulating factor** (**GM-CSF**) and a second polypeptide domain containing an antigenic polypeptide;
(2) an expression cassette (III) comprising (II);
(3) a transformed cell comprising (II);
(4) a DNA **vaccine** (IV) comprising (I), (II), or (III) and an excipient;
(5) a particle (V) comprising (II) or (III); and
(6) use of a composition containing (I), (II) or (III) and an excipient for preparing a pharmaceutical formulation for vaccinating a mammal against an antigen.
ACTIVITY - Antitumor.
MECHANISM OF ACTION - **Vaccine**; cytotoxic T cell response to an antigen, inducer.
To determine whether vaccination with the E7-HSP70 DNA construct protects mice against E7-expressing tumors, two in vivo tumor protection experiments were performed using different doses of DNA **vaccines**. For the first experiment, mice were vaccinated with 2 micro g naked DNA/mouse via a gene gun and boosted with the same dose one week later. For the second experiment, mice were vaccinated with 2 micro g naked DNA/mouse via a gene gun without a further booster. The mice were then challenged with 5 multiply 10 to the power of 4 TC-1/mouse subcutaneously in the right leg 7 days after the last vaccination. For the mice receiving vaccination with booster, 100% of those receiving E7-HSP70 DNA vaccination remained tumor-free 60 days after TC-1 challenge, while only 40% of mice receiving E7 DNA (in the absence of HSP-encoding DNA) vaccination remained tumor-free. In contrast, all of the unvaccinated mice and mice receiving empty plasmid or HSP DNA developed tumor growth within 15 days after tumor challenge. For the mice receiving vaccination once without booster, 100%

of those receiving E7-HSP70 DNA vaccination remained tumor-free 60 days after TC-1 challenge, whereas all of the unvaccinated mice and mice receiving empty plasmid, HSP70 DNA or E7 DNA developed tumor growth within 15 days after tumor challenge. These results indicated that a DNA construct encoding a MHC class I-restricted antigenic group operably linked to DNA encoding a HSP polypeptide, e.g. E7 HSP70 fusion DNA, significantly enhances the antitumor immunity against the growth of a tumor which express the class I-restricted group, e.g., TC-1 tumors.

USE - A composition (VI) comprising (I), (II), (III) or (IV) is useful for inducing an immune response such as a cytotoxic T cell response. The nucleic acid or vector encoding (I) present in the composition is administered as naked DNA by gene gun or equivalent, or by liposomal formulation. (VI) and (V) are thus useful for vaccinating a mammal against infection by inducing an immune response to a pathogen. Preferably (VI) and (V) are useful for vaccinating a mammal against a tumor antigen (claimed). The compositions and methods are useful for stimulating or enhancing the immunogenicity of a selected antigen or stimulating or enhancing a cellular immune response specific for that antigen.

ADVANTAGE - In contrast to standard DNA **vaccines**, the chimeric nucleic acid molecules and vaccination methods, yield potent antigen-specific immunotherapy. The polynucleotides and DNA **vaccines** can induce a cellular immune response that is at least 40 fold more potent than conventional DNA **vaccines**. The **vaccines** are safe and useful for administration to domesticated or agricultural animals, as well as humans, and have low immunogenicity. Dwg.0/20

L17 ANSWER 6 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-266112 [27] WPIDS
DNC C2001-080590
TI Replication selective adenovirus mutant with improved selectivity for tumor and hyperproliferative cells, for use in treating cancer and hypertension, comprises a deactivated or crippled early gene promoter.
DC B04 **D16**
IN MOLNAR-KIMBER, K; TOYOIZUMI, T
PA (UYPE-N) UNIV PENNSYLVANIA
CYC 94
PI WO 2001023004 A1 20010405 (200127)* EN 56p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001011909 A 20010430 (200142)
ADT WO 2001023004 A1 WO 2000-US27212 20001002; AU 2001011909 A AU 2001-11909 20001002
FDT AU 2001011909 A Based on WO 200123004
PRAI US 1999-157224 19990930
AB WO 200123004 A UPAB: 20010518
NOVELTY - A replication selective adenovirus (Ad) mutant (I), permitting Ad to spread through a tumor, which is under control of a tumor or tissue specific promoter, where the Ad early gene 1A (E1A) promoter has been deactivated or crippled to reduce activity of the promoter to a lower level than wild-type Ad, is new.

DETAILED DESCRIPTION - A new replication selective adenovirus (Ad) mutant (I) replicates 10-fold greater within cancer or hyperproliferative cells compared to a normal cell, permitting Ad to spread through a tumor, which is under control of a tumor or tissue specific promoter, where the Ad early gene 1A (E1A) promoter has been deactivated or crippled, reducing activity of the promoter to a lower level than wild-type Ad.

INDEPENDENT CLAIMS are also included for the following:

(1) introducing (I) to a target cell, by delivering the Ad vector to the target cell;

(2) delivering to a target cell a heterologous gene or gene fragment encoding a therapeutic peptide or polypeptide, by delivering the Ad vector to the cell;

(3) a target cell comprising (I);

(4) treating cancer, carcinoma, sarcoma, neoplasm, leukemia, lymphoma, or hyperproliferative disease comprising administering (I) to a patient;

(5) producing (II) an infectious, replication selective Ad particle, by:

(a) selecting a tumor specific promoter selected from a tumor that expresses a **tumor associated antigen**, which is active in an eukaryotic cell;

(b) deactivating or crippling Ad E1A promoter in a replication selective Ad, to reduce activity of the promoter to a lower level than that of wild-type replication selective Ad;

(c) introducing the promoter with the crippled replication selective Ad, to place the replication selective Ad under the control of **tumor associated antigen** promoter;

(d) culturing Ad construct under conditions permitting the uptake of Ad vector by and replication in a host cell expressing the **tumor associated antigen**; and

(e) harvesting the infectious, replication selective Ad particle produced by the host cells, where the resulting Ad particle is selectably reproduced only in cells expressing the **tumor associated antigen**;

(6) an Ad particle (III) produced by (II);

(7) inactivating (IV) a tumor or hyperproliferative target cell, in a patient, comprising steps (a)-(c) of (5), which provides a vector, introducing into the vector, a heterologous gene or gene fragment encoding a therapeutic peptide or polypeptide, such that it will be expressed from the vector within the target cell and introducing the vector into the target cell of the patient in a therapeutically effective amount; and

(8) a pharmaceutical composition comprising (III).

ACTIVITY - Cytostatic; hypotensive; vasotropic. The in vivo efficacy of viruses Ad460CEA and Ad522CEA were compared in xenogeneic tumor models in nude mice. In Ad460CEA, the CEA promoter replaced Ad nucleotides 460-522, upstream of the E1A genes and the blue fluorescent gene was present in the E3 region. In contrast, Ad522CEA had the CEA promoter inserted at nucleotide 522 and the blue fluorescent gene was present in the E3 region. Two tumor cell lines A549 (CEA positive) and HeLa (American Type Culture Collection) were inoculated subcutaneously into groups of 12 week old female NCR/NCI immunocompromised (nude mice). Tumors were injected with 100 micro l control media alone, 100 micro l containing 109

plaque forming units (pfu) of wild type Ad5 (Wt Ad5) or Ad5 containing thymidine kinase (TK) in the E3 region, or AdCEA460 or AdCEA522. The growth of the tumors was monitored and the volumes were calculated. Measurements indicated that Wt Ad5 and Ad522CEA treatments significantly reduced both tumor growth and tumor weight of both A549 and HeLa tumors in comparison to treatment with media alone. AdCEA460 reduced A549 tumor weight by 47 plus or minus 11 % in comparison to media control treatment group. In contrast, Ad460CEA did not significantly decrease the tumor weight of the HeLa tumors which express no or very low levels of CEA. These data indicated that deletion of the Ad5 sequences between nucleotide 460 and 522, i.e. elimination of several transcriptional regulatory elements, improved the specificity of the resulting replication selective Ad, Ad460CEA for CEA positive cells.

MECHANISM OF ACTION - Gene therapy; **vaccine**.

USE - (I) is useful for delivering a heterologous gene or gene fragment, suicide gene or therapeutic gene, including genes encoding for oncogenes, tumor suppressor gene, antisense and ribozyme RNAs, genes encoding enzymes, **cytokines** and other immune modulating macromolecules, recombinant antibodies, lytic peptides, **vaccine** antigens, macromolecules which complement genetic defects in somatic cells and macromolecules which analyze processes leading to cell death, to a target cell. (I) is further useful for treating a patient suffering from cancer, carcinoma, sarcoma, neoplasm, leukemia, lymphoma or hyperproliferative cell diseases, including restenosis, intimal proliferative disease and primary pulmonary hypertension (claimed).

ADVANTAGE - The heterologous gene or gene fragment encoding a therapeutic peptide or polypeptide achieves a direct, oncolytic effect on the target (claimed). (I) can propagate in cells that are positive for the relevant **tumor associated antigen**, eliminating the potential of recombination with the E1A sequences in 293 cells or PerC6 cells.

Dwg.0/5

L17 ANSWER 7 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-123319 [13] WPIDS
DNC C2001-035888
TI Immunogenic compositions comprising Flt-3 ligand encoding polynucleotide and one or more antigen, or **cytokine** encoding polynucleotides, useful for suppressing tumor growth and for treating autoimmune diseases (e.g. rheumatoid arthritis).
DC B04 **D16**
IN HERMANSON, G G
PA (VICA-N) VICAL INC
CYC 21
PI WO 2001009303 A2 20010208 (200113)* EN 149p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
ADT WO 2001009303 A2 WO 2000-US20679 20000731
PRAI US 1999-146170 19990730
AB WO 200109303 A UPAB: 20010307
NOVELTY - Immunogenic compositions comprising Flt-3 ligand encoding polynucleotide and one or more antigen or **cytokine** encoding polynucleotides, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are provided for:

(1) a composition (C1) comprising:

(a) 1 ng to 10 mg of a nucleic acid comprising a first polynucleotide

(N1) which hybridizes, at 42 deg. C in 50% formamide, 5 x SSC (saline sodium chloride), 50 mM sodium phosphate, 5 x Denhardt's solution, 10% dextran sulfate, and 20 micro g/ml denatured, sheared salmon sperm DNA, followed by washing at 65 deg. C in 0. 1 x SSC and 0. 1 % sodium dodecyl sulfate (SDS) (w/v), to a reference nucleic acid having a 839, 852, 1152, 663, 519, 1080, 537, or 859 (S1-S8, respectively) nucleotide sequence defined in the specification, or their complements, where the first polynucleotide encodes a polypeptide having immunity-enhancing activity when administered to a vertebrate;

(b) 1 ng to 30 mg of a nucleic acid (N2) comprising a second polynucleotide encoding one or more antigens, or one or more **cytokines**, where the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(2) a composition (C2) comprising:

(a) 1 ng to 10 mg of a nucleic acid comprising a first polynucleotide

(N3) which encodes a first polypeptide which, except for at least one but not more than 20 amino acid substitutions, deletions, or insertions, is identical to a second polypeptide selected from amino acids 28 to 163 of the 231 amino acid sequence (S9), amino acids 27 to 160 of 235 amino acid sequence (S15), or amino acids 27 to 185 of 235 amino acid sequence (S17) (all sequences are defined in the specification), where the first polypeptide has immunity-enhancing activity when administered to a vertebrate;

(b) 1 ng to 30 mg of N2, where the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(3) a pharmaceutical composition (C3) comprising:

(a) 1 ng to 10 mg of a nucleic acid molecule comprising a first polynucleotide (N4) encoding an amino acid sequence that is at least 90%, preferably 97%, identical to a reference amino acid sequence selected from

S9, 189 (S10), 220 (S11), 232 (S12), 172 (S14), S15, 178 (S16), S17 or 185

(S18) amino acid sequence defined in the specification, where % identity is determined using the Bestfit program with default parameters, and the polypeptide has immunity-enhancing activity when administered to a vertebrate;

(b) 1 ng to 30 mg of N2, where the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(4) a method (M1) for enhancing an immune response in a vertebrate, comprising administering C1, C2 or C3 to a tissue of the vertebrate, where

the first and second polynucleotides are expressed in vivo in an amount effective for a polypeptide expressed by the first polynucleotide to enhance the immunogenicity of one or more antigens, or one or more **cytokines**; and

(5) a method (M2) of suppressing tumor growth in a mammal, comprising

administering C1, C2 or C3 to a tissue of a mammal.

ACTIVITY - Antirheumatic; antiarthritic; immunostimulant; antiviral;

antibacterial; antifungal; antiparasitic; cytostatic; immunosuppressive; protozoacide; antiinflammatory.

Three groups of mice were used in the study. One group (n=9) was co-injected with VR6200 (a Flt-3 ligand-encoding plasmid) and VR1623 (bicistronic chimeric Id vector) (100 micro g each) on days 0, 14, and 28, and challenged with 500 38C13 tumor cells two weeks following the last injection. Control groups (n=10 each) were co-injected with VR1623 and VR1051 (control plasmid), or VR1605 (generic cloning vector comprising the constant regions of human kappa light chain and gamma 1 heavy chain separated by a CITE (cap independent translational enhancer)) or alone (200 micro g) on days 0, 14, and 28, and challenged with 500 38C13 tumor cells two weeks following the last injection.

The co-injection of a Flt-3 ligand-encoding plasmid (100 micro g of VR6200) with a tumor-specific antigen-encoding plasmid (100 micro g of VR1623) significantly enhanced protection from tumor challenge. Eight out of nine mice injected with VR1623 and VR6200 survived the challenge as compared to zero out of ten mice surviving after being immunized with VR1623 and the control plasmid, VR1051. This increased survival was statistically significant p=0.00007. Furthermore, the co-injection of a Flt-3 ligand-encoding plasmid (VR6200) with an idiotype antigen-encoding plasmid (VR1623) resulted in greatly enhanced anti-Id antibody titer relative to mice injected with VR1623 and VR1051, or with VR1623 alone.

MECHANISM OF ACTION - **Vaccine.**

USE - The compositions are useful for suppressing tumor growth in a mammal. The tumor is melanoma, glioma or lymphoma, particularly B-cell lymphoma. The compositions are used in conjunction with additional cancer treatments (claimed).

The immunogenic compositions can also be used for the prophylactic and/or therapeutic treatment of:

(a) bacterial (e.g. Bacillus infections), viral (e.g. hepatitis B and C in humans), parasitic (e.g. malaria) and fungal infections;

(b) autoimmune diseases (e.g. rheumatoid arthritis and osteoarthritis);

(c) cancer (e.g. cancers of stomach, small intestine, liver, etc.); and

(d) Aujeszky's disease in pigs.

Various other examples of these diseases are given in the specification.

Dwg.0/9

L17 ANSWER 8 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-049897 [06] WPIDS
DNC C2001-013723
TI Stimulating a systemic antitumor immune response, useful for treatment or prevention, by administering tumor cells modified to express **granulocyte-macrophage colony-stimulating factor.**
DC B04 D16
IN DRANOFF, G; HARDY, S
PA (CELL-N) CELL GENESYS INC
CYC 92
PI WO 2000072686 A1 20001207 (200106)* EN 109p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG
SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000054585 A 20001218 (200118)

ADT WO 2000072686 A1 WO 2000-US15190 20000602; AU 2000054585 A AU 2000-54585 20000602

FDT AU 2000054585 A Based on WO 200072686

PRAI US 1999-324707 19990602

AB WO 200072686 A UPAB: 20010126

NOVELTY - Stimulating a systemic immune response to a tumor, or its antigen (Ag), in a mammal, comprising administering a **proliferation-incompetent** tumor cell (A) genetically modified to express **granulocyte-macrophage colony-stimulating factor** (**GM-CSF**), is new.

DETAILED DESCRIPTION - Stimulating a systemic immune response to a tumor, or its antigen (Ag), in a mammal, comprising administering a **proliferation-incompetent** tumor cell (A) genetically modified to express **granulocyte-macrophage colony-stimulating factor** (**GM-CSF**), is new. (A) is the same type as the tumor being treated, expresses Ag and is modified using a recombinant virus (RV), i.e. adeno, lenti, adeno-associated, SV40, herpes or vaccinia virus, containing the **GM-CSF** sequence.

INDEPENDENT CLAIMS are also included for the following:

(1) RV;

(2) (A) transformed with RV and able to express **GM-CSF**; and

(3) kits for stimulating a systemic immune response to tumor or Ag in a mammal comprising RV and a container for holding a (portion of) tumor tissue.

ACTIVITY - Cytostatic.

B16 melanoma cells were transformed to express **GM-CSF** and interleukin-2, then used for subcutaneous immunization of mice. The animals were challenged with normal B16 cells and 6 of 10 did not develop tumors. When the implanted cells also expressed interleukin-4, 9 of 10 test animals remained free of tumor.

MECHANISM OF ACTION - Stimulation of specific systemic immune response; **vaccine**.

USE - The method is used to inhibit formation of tumors, and to cause regression, or retard growth, of pre-existing tumors. Non-small cell lung cancer cells were isolated from patients, transformed with a replication-deficient adenovirus that expressed human **GM-CSF**, irradiated and then used to inoculate the donors, several times at 7-14 day intervals and at doses of 1-10 million cells, intradermally. Development of a delayed hypersensitivity reaction provided evidence for an antitumor response and one patient showed a 50 % reduction in lung and lymph node metastases. Two patients (for whom the inoculating cells were obtained by resection of isolated metastases) remained free of disease for 9-10 months and two other patients for 3 months.

Dwg.0/19

L17 ANSWER 9 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-024946 [03] WPIDS
DNC C2001-007621
TI Antigenic composition having an antigen (e.g. viral protein) and an adjuvant, useful for enhancing humoral and cellular immune response in a host or as a prophylaxis against virus, bacterium, parasite, cancer cell or allergen.
DC B04 C06 **D16**
IN HAGEN, M
PA (AMCY) AMERICAN CYANAMID CO
CYC 90
PI WO 2000069456 A2 20001123 (200103)* EN 129p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000048473 A 20001205 (200113)
ADT WO 2000069456 A2 WO 2000-US13156 20000512; AU 2000048473 A AU 2000-48473 20000512
FDT AU 2000048473 A Based on WO 200069456
PRAI US 1999-133963 19990513
AB WO 200069456 A UPAB: 20010116
NOVELTY - An antigenic composition comprising an antigen from a pathogenic virus, bacterium, fungus or parasite, a cancer or tumor cell, an allergen, or an amyloid peptide protein, and an adjuvant is new.
DETAILED DESCRIPTION - An antigenic composition comprising an antigen from a pathogenic virus, bacterium, fungus or parasite, a cancer or tumor cell, an allergen, or an amyloid peptide protein, and an adjuvant is new. The adjuvant is a combination of (1) 3-O-deacylated monophosphoryl lipid A or monophosphoryl lipid A, their derivatives or analogs, and (2) a **cytokine** or lymphokine, their agonist or antagonist, which enhances the immune response to the antigen in a vertebrate host.
INDEPENDENT CLAIMS are also included for the following:
(1) methods for increasing the ability of an antigenic composition containing an antigen from a pathogenic virus (e.g. human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), or human Respiratory syncytial virus (RSV) antigen), bacterium (e.g. Neisseria gonorrhoeae), fungus or parasite to elicit the immune response of a vertebrate host, comprising administering to the host the antigenic compositions;
(2) methods for increasing the ability of an antigenic composition containing an antigen from a pathogenic virus (e.g. HIV or SIV antigen), bacterium (e.g. N. gonorrhoeae), fungus or parasite to elicit cytotoxic T lymphocytes in a vertebrate host, comprising administering to the host the antigenic compositions;
(3) a method for increasing the ability of an antigenic composition containing a cancer **antigen** or **tumor-associated antigen** from a cancer cell or tumor cell to elicit a therapeutic or prophylactic anti-cancer effect in a vertebrate

host, comprising administering to the host the antigenic composition;

(4) a method for increasing the ability of an antigenic composition containing a selected allergen to moderate an allergic response in a vertebrate host, comprising administering to the host the antigenic composition comprising the allergen; and

(5) a method for increasing the ability of an antigenic composition to prevent or treat disease characterized by amyloid deposition in a vertebrate host, comprising administering to the host a polypeptide, peptide or fragment derived from amyloid peptide protein, or an antibody.

ACTIVITY - Immunostimulant; cytostatic; antiallergic.

MECHANISM OF ACTION - **Vaccine.**

Balb/c mice immunized subcutaneously with the C4/V3 HIV peptide T1SP10MN (A) (-Cys), formulated with MPL (RTM) SE and **GM-CSF**, produced serum IgG titers in excess of 107 after only two injections. The antibody response was HIV-neutralizing, and demonstrated significant increases in IgG1, IgG2a and IgG2b peptide-specific antibody titers. Spleen cells stimulated in culture with the peptide released elevated levels of IL-4, IL-5 and interferon-gamma. Collectively, these findings were indicative of the induction of a balanced Th1/Th2-type response. IgG and IgA antibodies were generated that were specific for T1SP10MN (A) (-Cys) in the vaginal lavage fluids of mice immunized with MPL (RTM) SE and **GM-CSF**. These findings also indicated that the combination of MPL (RTM) SE and **GM-CSF** with an HIV-peptide antigen results in the induction of a favorable immune response profile.

USE - The antigenic composition is useful for enhancing both the humoral and cellular immune response in a vertebrate host to a selected antigen. In particular, the composition is useful for enhancing the hosts immune response or as a prophylaxis against virus, bacterium, fungus or parasite, cancer or tumor cell, allergen, or amyloid peptide protein.

Dwg.0/5

L17 ANSWER 10 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-587476 [55] WPIDS
DNC C2000-175273
TI Use of Klebsiella membrane fraction as adjuvant, for e.g. antitumor or antiviral **vaccines**, to direct a Th1, or mixed, immune response against associated antigen.
DC B04 **D16**
IN BECK, A; BONNEFOY, J Y; CORVAIA, N; LIBON, C; N GUYEN, T; BONNEFOY, J; N'GUYEN, T N
PA (FABR) FABRE MEDICAMENT SA PIERRE
CYC 26
PI WO 2000054789 A1 20000921 (200055)* FR 35p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BR CA CN JP MX US ZA
FR 2790959 A1 20000922 (200055)
AU 2000032980 A 20001004 (200101)
ADT WO 2000054789 A1 WO 2000-FR622 20000315; FR 2790959 A1 FR 1999-3153 19990315; AU 2000032980 A AU 2000-32980 20000315
FDT AU 2000032980 A Based on WO 200054789
PRAI FR 1999-3153 19990315
AB WO 200054789 A UPAB: 20001102
NOVELTY - Use of a membrane fraction (A) from Klebsiella pneumoniae, associated with an antigen or hapten (I), for preparation of a pharmaceutical composition that directs a Th1, or mixed Th1/Th2 immune response against (I), is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a pharmaceutical composition comprising (A) associated with (I).

ACTIVITY - Cytostatic; virucide; antibacterial; antifungal; antiparasitic.

The recombinant protein BBG2Na (comprising the 101 amino acid peptide, G2Na, from the G protein of respiratory syncytial virus (RSV) and the C-terminal fragment of protein G of streptococcus) was used to immunize mice (two 20 micro g subcutaneous injections), in combination with various amount of a membrane fraction (A) from Klebsiella pneumoniae.

Blood samples analyzed after 28 days showed a significant increase in IgG response to G2Na, relative to administration of BBG2Na in saline, comparable to that induced by alum or Freund's adjuvant. In presence of 0.1 mg (A), titers of IgG1 and IgG2a were roughly the same; contrast alum and Freund's adjuvant which strongly favored an IgG1 response. Three weeks after the second immunization, the mice were challenged with 105 TCID50 of type A RSV. Examination of lungs after a further 5 days showed that the animals had been protected against infection.

MECHANISM OF ACTION - Induction of a specific immune response.

USE - The (A)/(I) product is used for treatment or prevention of infectious diseases (viral, bacterial, fungal or parasitic) or cancers, most especially infections by paramyxoviruses, specifically respiratory syncytial virus or parainfluenza.

ADVANTAGE - (A) not only increases the antibody response to (I), but also directs the **cytokine** response towards a Th1(or mixed, Th1/Th2) type, especially favoring production of Ig2a subtype antibodies.

Dwg.0/4

L17 ANSWER 11 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-558170 [51] WPIDS
CR 2000-303749 [26]
DNC C2000-166157
TI Recombinant polynucleotide for use in cancer **vaccines** and in adoptive immunotherapy comprises a plurality of polynucleotides, encoding an identical antigenic peptide, operatively linked to each other.
DC B04 **D16**
IN NICOLETTE, C A; SHANKARA, S
PA (GENZ) GENZYME CORP
CYC 86
PI WO 2000047229 A2 20000817 (200051)* EN 72p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 2000029926 A 20000829 (200062)
ADT WO 2000047229 A2 WO 2000-US3655 20000210; AU 2000029926 A AU 2000-29926 20000210
FDT AU 2000029926 A Based on WO 200047229
PRAI US 1999-162170 19991028; US 1999-120002 19990211; US 1999-161845 19991027
AB WO 200047229 A UPAB: 20001016

NOVELTY - A recombinant polynucleotide (I) comprising a plurality of polynucleotides encoding an identical antigenic peptide, which are operatively linked to each other to enhance their translation and binding of the peptide to major histocompatibility complex (MHC) molecules, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a gene delivery vehicle comprising (I);

(2) a host cell comprising (I);

(3) presenting antigenic epitopes on the surface of an antigen presenting cell comprising introducing (I) so that the antigenic peptide is translated and presented on the surface of the cell;

(4) generating educated immune effector cells comprising culturing (2) with naive immune effector cells so that they proliferate at the expense (2);

(5) an educated immune effector cell, which has been cultured in the presence and at the expense of (2); and

(6) modulating an immune response in a subject comprising administering (I), (2), or (5).

ACTIVITY - Immunomodulatory; cytostatic; antibacterial; virucide. No suitable biological data is given.

MECHANISM OF ACTION - **Vaccine**; gene therapy. No suitable biological data is given.

USE - (I), a host cell comprising (I), or an educated immune effector cell that has been cultured in the presence and at the expense of the host cell are used to modulated an immune response in a subject (claimed). (I) is useful in cancer **vaccines** an in adoptive immunotherapy. (I) can also induce T cell anergy for use in autoimmune disorders. An immune response against a pathogen such as a virus or bacteria can also be induced. (I) is also used in assays for predicting the in vivo efficacy of (I), determining the precursor frequency of immune effector cells specific for an antigenic peptide produced by (I), and monitoring the efficacy of (I) once it has been used to modulate an immune response.

ADVANTAGE - There is more potent antigen presentation by cells that express multiple copies of an epitope (i.e. that contain (I)) than ones with a single copy. Cells infected with a vector comprising (I) are lyzed more efficiently than cells infected with a virus encoding a single epitope.

Dwg.0/10

L17 ANSWER 12 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-387795 [33] WPIDS
DNC C2000-117799
TI **Vaccine** specific for cell-surface receptor antigen, useful e.g. for treating cancer, comprises genetic construct expressing antigen and two immune response-modifying agents.
DC B04 **D16**
IN DISIS, M L; HELLSTROM, I; HELLSTROM, K E; SCHOLLER, N B
PA (PACI-N) PACIFIC NORTHWEST RES FOUND
CYC 90
PI WO 2000029582 A2 20000525 (200033)* EN 64p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000031015 A 20000605 (200042)
ADT WO 2000029582 A2 WO 1999-US27404 19991117; AU 2000031015 A AU 2000-31015 19991117
FDT AU 2000031015 A Based on WO 200029582
PRAI US 1999-441411 19991116; US 1998-109106 19981118
AB WO 200029582 A UPAB: 20010410
NOVELTY - **Vaccine** (A) for eliciting, or increasing the titer of, antibodies specific for a cell-surface receptor antigen (Ag), comprises a recombinant expression construct (EC) that contains at least one promoter,
at least one sequence (I) encoding Ag, and nucleic acid sequences encoding
different immune response-altering molecules (IRAM) that are accessory cell agents or T cell agents.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a **vaccine** (A1) for eliciting, or enhancing Ag specific antibody titer, containing a first EC expressing Ag and an IRAM, and second EC expressing an IRAM;
(2) a **vaccine** (A2) for eliciting, or enhancing Ag specific antibody titer, containing three EC, each expressing one of Ag, the two IRAMs of the novelty;
(3) a **vaccine** (A3) for eliciting, or enhancing Ag specific antibody titer, containing an EC expressing Ag and a second EC expressing both (1) and (2); and
(4) a **vaccine** comprising the expression products of any of the EC in (A)-(A3).
ACTIVITY - Anticancer.
MECHANISM OF ACTION - **Vaccine**.
USE - (A), and the expression products of EC, are used to generate an
immune response against particularly **tumor-associated antigens**.
ADVANTAGE - (A) induce specific antibodies at sustained and high titers, even in subjects who would normally be unable to mount a strong antibody response. The **vaccines** provide co-ordinated expression of Ag, stimulation of T cell activity and mediation of accessory cell function.
Dwg.0/3

L17 ANSWER 13 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-365752 [31] WPIDS
DNN N2000-273655 DNC C2000-110573
TI Treating and diagnosing cancer comprises contacting serum samples obtained
before and after **vaccine** treatment with an array of proteins from a biological sample.
DC B04 **D16** S03
IN ANDO, D; CHANG, J; MCARTHUR, J; ROBERTS, M; SIMONS, J
PA (CELL-N) CELL GENESYS INC
CYC 80
PI WO 2000026676 A1 20000511 (200031)* EN 92p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW

AU 2000013409 A 20000522 (200040)

ADT WO 2000026676 A1 WO 1999-US25936 19991103; AU 2000013409 A AU 2000-13409 19991103

FDT AU 2000013409 A Based on WO 200026676

PRAI US 1998-106795 19981103

AB WO 200026676 A UPAB: 20000630

NOVELTY - A method for obtaining a **tumor-associated antigen** (TAA) is new.

DETAILED DESCRIPTION - The method comprises;

(a) preparing an array of proteins from a biological sample;

(b) obtaining a first and second serum sample from a subject before and after, respectively, treatment with a **vaccine** comprising **proliferation incompetent** tumor cells expressing **GM-CSF** and the TAA;

(c) contacting a first sample of the proteins in (a) with the first serum sample;

(d) contacting a second sample of the proteins in (a) with the second serum sample; and

(e) identifying a protein in the array that reacts with the second serum sample but not the first.

INDEPENDENT CLAIMS are also included for the following;

(1) screening for the presence of a TAA comprising;

(a) isolating the TAA identified in the method above;

(b) preparing an antibody against TAA;

(c) contacting the biological specimen with the antibody in (b); and

(d) detecting the presence of an antigen-antibody complex.

(2) a kit for screening the presence of a TAA in a biological sample comprising;

(a) unlabelled first antibodies against a TAA reactive with serum from an individual treated with a **vaccine** comprising **proliferation incompetent** tumor cells expressing the TAA and **GM-CSF**, but not reactive with a pre-treatment serum sample;

(b) a solid support for adhering the biological sample; and

(c) labelled second antibodies against the first antibodies.

ACTIVITY - Cytostatic; antiproliferative.

MECHANISM OF ACTION - The **vaccine** increases the expression of the **tumor associated antigens** and enables the identification of tumor cells by the immune system of the affected individual. No data given.

USE - The method is useful for the identification of **tumor-associated antigens**.

DESCRIPTION OF DRAWING(S) - The drawing is a schematic representation of the MFG vector containing a **cytokine**-encoding sequence.

Dwg.1/18

L17 ANSWER 14 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2000-317604 [27] WPIDS

DNC C2000-096060

TI Generating T-cells reactive to an antigenic molecule comprises contacting T-cells and antigen-presenting cells in vitro with a heat shock protein and an antigenic molecule complex.
DC B04 **D16**
IN SRIVASTAVA, P K
PA (UYCO-N) UNIV CONNECTICUT HEALTH CENT
CYC 86
PI WO 2000019828 A1 20000413 (200027)* EN 85p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9965052 A 20000426 (200036)
ADT WO 2000019828 A1 WO 1999-US22856 19991004; AU 9965052 A AU 1999-65052 19991004
FDT AU 9965052 A Based on WO 200019828
PRAI US 1998-166401 19981005
AB WO 200019828 A UPAB: 20000606
NOVELTY - Generating T cells reactive to an antigenic molecule (A) by contacting T cells and antigen presenting cells (immune cells) in vitro with a purified non-covalent complex (I) of a heat shock protein (HSP) and
an antigenic molecule, where the immune cells are from an animal immunized
with a molecule displaying the antigenicity of the antigenic molecule, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) generating T cells reactive to an antigenic molecule comprising:
(a) immunizing an animal with an antigenic molecule;
(b) obtaining immune cells comprising T cells and antigen presenting cells (APCs) from the animal; and
(c) incubating the cells in vitro with (I);
(2) generating T cells reactive to an antigenic molecule comprising:
(a) immunizing immune cells in vitro with an antigenic molecule; and
(b) incubating the immune cells in vitro with (I);
(3) expanding T cells reactive to an antigenic molecule comprising contacting immune cells from an animal immunized with a molecule displaying the antigenicity of the antigenic molecule, with APCs pulsed with a purified HSP-antigenic molecule complex, where the APCs and immune cells have at least 1 common MHC allele;
(4) expanding T cells reactive to an antigenic molecule comprising:
(a) immunizing an animal with an antigenic molecule;
(b) obtaining immune cells (comprising T cells) from the animal; and
(c) contacting the immune cells with APCs pulsed with a purified (I),
where the APCs and immune cells have at least 1 common MHC allele;
(5) treating or preventing a disease or disorder in a subject comprising the steps of:
(a) generating T cells reactive to an antigenic molecule as in (A); and
(b) administering an effective amount of the antigen-reactive T cells
to the subject; and
(6) a composition comprising T cells reactive to an antigenic

molecule generated by the method of (1).

ACTIVITY - Cytostatic; immunostimulatory; antiviral; antibacterial; antifungal; antiparasitic.

MECHANISM OF ACTION - **Vaccine**.

USE - The methods are useful for producing antigen reactive T-cells. The T-cells and compounds containing them are useful for treating or preventing viral diseases, (e.g. those caused by hepatitis A, B, or C, influenza, herpes virus, cytomegalovirus, coxsachie virus, rubella virus, polio virus, HIV, rhinovirus, adenovirus, and papova virus), bacterial diseases (e.g. those caused by Mycobacteria rickettsia, Mycoplasma, Neisseria, and Legionella), protazoal diseases (e.g. those caused by Leishmania, Kokzidioa, and Trypanosoma), and parasitic diseases (e.g. those caused by Chlamydia, and Rickettsia), and cancer.

Dwg.0/10

L17 ANSWER 15 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-147241 [13] WPIDS
DNC C2000-046091
TI Use of poxvirus in immunogenic compositions for prevention or treatment of tumors and microbial infections, provides synergistic increase in the immune response.
DC B04 **D16**
IN CHEVALIER, M; MEIGNIER, B; MOSTE, C; SAMBHARA, S
PA (INMR) PASTEUR MERIEUX SERUMS & VACCINS SA; (AVET) AVENTIS PASTEUR
CYC 85
PI WO 2000000216 A2 20000106 (200013)* EN 62p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9950368 A 20000117 (200026)
EP 1087789 A2 20010404 (200120) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
ADT WO 2000000216 A2 WO 1999-EP4913 19990628; AU 9950368 A AU 1999-50368 19990628; EP 1087789 A2 EP 1999-934677 19990628, WO 1999-EP4913 19990628
FDT AU 9950368 A Based on WO 200000216; EP 1087789 A2 Based on WO 200000216
PRAI EP 1998-420111 19980626; EP 1998-420110 19980626
AB WO 200000216 A UPAB: 20000313

NOVELTY - Use of a poxvirus (A), to increase the specific immune response in a vertebrate to an immunogenic compound (I) and for the preparation of a composition containing (I) is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a composition containing (I) and (A) that encodes a heterologous polypeptide (II), i.e. an adhesion or co-stimulatory molecule, chemokine, apoptotic factor, **cytokine** or growth hormone; and

(2) compositions containing, as (I), a polypeptide (Ia) or a DNA plasmid that encodes (Ia), and (A) that encodes a heterologous polypeptide with the same amino acid sequence as (Ia).

ACTIVITY - Antiviral; antibacterial; antiparasitic; antitumor.

MECHANISM OF ACTION - Induction of a specific immune response.

USE - The compositions are used to induce a protective or (not claimed) therapeutic immune response (cellular and humoral) against

pathogenic microorganisms (viruses, bacteria or eukaryotic pathogens) or tumors, specifically against human immune deficiency virus or influenza virus. Mice were immunized twice with a combination of 3 mu g A/Texas influenza **vaccine** and 20 million CCID50 of ALVAC poxvirus. Three weeks after the booster injection, the animals were challenged with a normally lethal dose of live influenza virus. Four of 6 treated animals survived; compare 1 of 6 for animals given only the A/Texas **vaccine** and 0 of 6 for those given only the ALVAC virus.

ADVANTAGE - (A) provides a synergistic improvement in the immune response to (I). A single (I)-(A) composition provides as good a response as that produced by the prime-boost protocol which requires two separate formulations. Particularly the use of (A) improves response to influenza **vaccines** in the elderly. Guinea pigs were injected intramuscularly, on days 0 and 29, with 106.1 CCID50 of vCP205 (an ALVAC canarypox vector containing a sequence encoding HIV env, gag and protease (described in WO9527507) and 40 mu g of recombinant gp160 from the HIV strains MN and LAI. The antibody response to both gp160 and the V3 domain was better in these animals than in controls vaccinated with vCP205 or gp160 alone, or with these two components in separate administrations (the prime-boost protocol).

Dwg.0/15

L17 ANSWER 16 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-039276 [03] WPIDS
CR 2000-024571 [01]
DNC C2000-010251
TI Composition for inducing tumor-specific immune response, useful for immunotherapy of neoplasia in vertebrates.
DC B04 **D16**
IN PACHMANN, K; ROEHNISCH, T
PA (IMMU-N) IMMUNOGENEC BIOTECHNOLOGIE GMBH
CYC 24
PI WO 9959624 A2 19991125 (200003)* DE 57p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA IL JP US
AU 9941442 A 19991206 (200019)
EP 1077720 A2 20010228 (200113) DE
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9959624 A2 WO 1999-EP3380 19990517; AU 9941442 A AU 1999-41442 19990517; EP 1077720 A2 EP 1999-924991 19990517, WO 1999-EP3380 19990517
FDT AU 9941442 A Based on WO 9959624; EP 1077720 A2 Based on WO 9959624
PRAI WO 1999-EP3353 19990514; DE 1998-19821925 19980515
AB WO 9959624 A UPAB: 20010307
NOVELTY - A composition (I) comprising a phage or functionally equivalent fragment expressing at least one tumor-specific and/or **tumor-associated antigen** as a fusion protein, with a phage coat protein or derivative on its surface, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for the production of (I), comprising:

(1) extraction of DNA from an individual tumor cell, so that the gene encoding the tumor-specific antigen can be amplified;

(2) cloning, after digestion of the gene in a vector system with restriction enzymes and gel electrophoresis; and

(3) expression of the gene as a phage fusion protein.

ACTIVITY - Cytostatic; immunospecific.

MECHANISM OF ACTION - Immunostimulant; **vaccine**.
USE - (I) is useful for the production of a treatment to induce a specific immune response, preferably for specific immunotherapy of a neoplasia in vertebrates (claimed).
Dwg.0/5

L17 ANSWER 17 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-620288 [53] WPIDS
DNC C1999-181049
TI Enhancing mammalian immune response, useful for treating individuals suffering from an immuno-compromised disease or disorder e.g. AIDS and/or for use with chemotherapy recipients.
DC B04 **D16**
IN BRENNER, M B; DASCHER, C C; HIROMATSU, K; PORCELLI, S A
PA (BGHM) BRIGHAM & WOMENS HOSPITAL INC; (BGHM) BRIGHAM WOMENS HOSPITAL INC
CYC 86
PI WO 9952547 A1 19991021 (199953)* EN 49p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9935588 A 19991101 (200013)
EP 1071452 A1 20010131 (200108) EN
R: AT BE DE ES FI FR GB IE IT SE
ADT WO 9952547 A1 WO 1999-US8112 19990413; AU 9935588 A AU 1999-35588 19990413; EP 1071452 A1 EP 1999-917473 19990413, WO 1999-US8112 19990413
FDT AU 9935588 A Based on WO 9952547; EP 1071452 A1 Based on WO 9952547
PRAI US 1998-81638 19980413
AB WO 9952547 A UPAB: 19991215
NOVELTY - A method of enhancing an immune response in a mammal to at least one CD1 antigen is new and comprises co-administering to the mammal an effective amount of at least one CD1 antigen and at least one T cell stimulating compound.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a method of vaccinating a mammal against at least one CD1 antigen comprising administering to the mammal an effective amount of at least one CD1 antigen and at least one adjuvant;
(2) a method of stimulating a CD1-restricted immune response in a mammal comprising administering to the mammal a composition comprising at least one adjuvant and at least one lipid antigen where the antigen elicits a CD1-restricted immune response;
(3) an immunogenic composition (I), comprising:
(a) at least one T cell stimulating compound; and
(b) at least one CD1 antigen, where the CD1 antigen elicits a CD1-restricted immune response;
(4) a method for eliciting an immunogenic response in a mammal comprising administering (I);
(5) a **vaccine** composition (II) comprising at least one adjuvant and at least one lipid antigen where the lipid antigen elicits a CD1-restricted immune response;
(6) a method for vaccinating a mammal comprising administering (II);

and

(7) a kit comprising at least one T-cell stimulating compound and at least one CD1 antigen where the CD1 antigen elicits a CD1-restricted immune response.

ACTIVITY - Anti-parasitic; antibacterial; immune stimulant.

MECHANISM OF ACTION - The method elicits at least one immunological parameter e.g. antibody response the antigen, cytotoxic T-lymphocyte response, T-cell proliferation, helper T-cell response or a T-cell modulated **cytokine** response.

USE - The method is useful for enhancing or boosting the immune response of an individual who has a immuno-compromised disease, disorder or condition (e.g. AIDS or chemotherapy recipient). The method is also useful for eliciting or boosting an immune response for at least one bacterial infection (e.g. Mycobacteria genus, Hemophilus genus, Streptococcus genus, Staphylococcus genus and Chlamydia) and/or at least one parasitic infection (e.g. Plasmodium or Trypanosoma genus). (All claimed). The CD1 **antigen** can also be a **tumor associated** or derived **antigen** that is involved in diseases e.g. cancer (e.g. melanoma, breast cancer, prostate cancer, and colo-rectal cancer) or a self antigen that is involved in autoimmune diseases (e.g. diabetes, Lupus, rheumatoid arthritis).

ADVANTAGE - The method enhances the immune response for **vaccines** without eliciting a sufficient protective immune response in a host.

Dwg.0/7

L17 ANSWER 18 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-590956 [50] WPIDS
DNC C1999-172475
TI Preparing cells for use as cancer **vaccines** and in adoptive immunotherapy.
DC B04 **D16**
IN KAPLAN, J; NICOLETTE, C A
PA (GENZ) GENZYME CORP
CYC 23
PI WO 9947102 A2 19990923 (199950)* EN 65p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 9931023 A 19991011 (200008)
EP 1063891 A2 20010103 (200102) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9947102 A2 WO 1999-US6031 19990319; AU 9931023 A AU 1999-31023 19990319; EP 1063891 A2 EP 1999-912710 19990319, WO 1999-US6031 19990319
FDT AU 9931023 A Based on WO 9947102; EP 1063891 A2 Based on WO 9947102
PRAI US 1998-78880 19980320
AB WO 9947102 A UPAB: 19991201
NOVELTY - A genetically modified antigen-presenting cell (APC) (I) expressing a polynucleotide coding for a peptide having herpes simplex virus (HSV) ICP47 biological activity and presenting exogenous antigen on a major histocompatibility complex (MHC) class I molecule is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a substantially pure population of immune effector cells (II) grown in the presence and expense of (I); and

(2) preparation of (I) and (II).

ACTIVITY - Cytostatic; immunomodulatory.

MECHANISM OF ACTION - **Vaccine**.

USE - APC (I) is useful for inducing an immune response (claimed) against an antigen in a patient (adoptive immunotherapy), especially as **vaccines** against cancer in mammals, preferably humans. The cells are also useful for expanding populations of immune effector cells (preferably cytotoxic T lymphocyte (CTL) cells) by growing them in the presence of (I) (claimed). (I) can be used to screen for agents having ability to induce an immune response

ADVANTAGE - Prior art methods which enhance self-class MHC I molecule expression do not always increase the immunogenic potency of a tumor when used as **vaccines**, with or without adjuvant. The present invention will enhance antigen presentation by antigen-presenting cells when used as **vaccines** or therapies.

Dwg.0/7

L17 ANSWER 19 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-561746 [47] WPIDS
DNC C1999-163706
TI Pure population of antigen-specific immune effector cells for use in immunotherapy of tumors.
DC B04 **D16**
IN GREGORY, R J; KAPLAN, J
PA (GENZ) GENZYME CORP
CYC 23
PI WO 9946992 A1 19990923 (199947)* EN 64p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 9931029 A 19991011 (200008)
EP 1071333 A1 20010131 (200108) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9946992 A1 WO 1999-US6039 19990319; AU 9931029 A AU 1999-31029 19990319; EP 1071333 A1 EP 1999-912716 19990319, WO 1999-US6039 19990319
FDT AU 9931029 A Based on WO 9946992; EP 1071333 A1 Based on WO 9946992
PRAI US 1998-78889 19980320
AB WO 9946992 A UPAB: 19991116
NOVELTY - Pure population of educated, antigen-specific immune effector cells (A) produced by culturing naive immune effector cells (B) with antigen-presenting cells (APCs) that express a heterologous or altered antigen (Ag), distinct from the corresponding native self antigen (sAg).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) composition comprising (A) and a carrier; and

(2) inducing an immune response to sAg by administering Ag or an APC that expresses Ag.

ACTIVITY - Antitumor.

MECHANISM OF ACTION - Ag break the immunological tolerance of sAg by induction of a cross-reactive response to Ag. Mice were immunized against the melanoma antigen gp100 by intravenous injection of 0.5 million bone marrow dendritic cells transduced with an adenoviral vector that expressed murine or human gp100. Two weeks later they were challenged with 20000 B16 melanoma cells (subcutaneously) and growth of tumors monitored. For animals expressing the murine gp100 only 1 of 5 was free of tumor after 40 days, compared with 3 or 4 of 5 (two tests) for those given the human protein.

USE - (A) are used in adoptive immunotherapy, and as **vaccines** , for treatment and prevention of tumors. Also Ag, or APCs that express them, are used to induce an immune response that is cross-reactive with sAg.
Dwg.0/4

L17 ANSWER 20 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-494293 [41] WPIDS
DNC C1999-144897
TI New protein derivatives used in cancer **vaccine** therapy for treating a range of cancers including melanomas, carcinomas and cancers of breast.
DC B04 **D16**
IN BASSOLS, C V; COHEN, J; SILVA, T C; SLAQUI, M M; CABEZON, S T; SLAOUI, M; VINALS, B C; CABEZON SILVA, T; VINALS BASSOLS, C; SLAOUI, M M
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 86
PI WO 9940188 A2 19990812 (199941)* EN 74p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9927220 A 19990823 (200005)
ZA 9900872 A 20000927 (200050) 75p
NO 2000003958 A 20001004 (200058)
EP 1053325 A2 20001122 (200061) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
BR 9907691 A 20001114 (200064)
CZ 2000002869 A3 20010117 (200107)
ADT WO 9940188 A2 WO 1999-EP660 19990202; AU 9927220 A AU 1999-27220 19990202;
ZA 9900872 A ZA 1999-872 19990204; NO 2000003958 A WO 1999-EP660 19990202,
NO 2000-3958 20000804; EP 1053325 A2 EP 1999-907476 19990202, WO 1999-EP660 19990202; BR 9907691 A BR 1999-7691 19990202, WO 1999-EP660 19990202; CZ 2000002869 A3 WO 1999-EP660 19990202, CZ 2000-2869 19990202
FDT AU 9927220 A Based on WO 9940188; EP 1053325 A2 Based on WO 9940188; BR 9907691 A Based on WO 9940188; CZ 2000002869 A3 Based on WO 9940188
PRAI GB 1998-2650 19980206; GB 1998-2543 19980205
AB WO 9940188 A UPAB: 19991011
NOVELTY - **Tumour-associated antigen** derivatives (A) obtained from MAGE (melanoma antigen) family are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) nucleic acid sequence encoding (A);
(2) a vector comprising the nucleic acid of (1);
(3) a host cell transformed with the vector of (2);
(4) a **vaccine** containing (A) or the nucleic acid of (1);
(5) a purification process of MAGE protein or its derivatives comprises:
(a) reducing disulfide bonds;
(b) blocking resulting free thiol group with a blocking group; and
(c) subjecting the resulting derivative to one or more chromatographic purification steps;

(6) a process for **vaccine** production comprises:
(a) purification of MAGE protein or its derivative by the process of (5); and
(b) formulating the resulting protein as a **vaccine**.
ACTIVITY - Cytostatic
MECHANISM OF ACTION - **Vaccine**.
The **vaccine** Lipo D 1/3 Mage 3 His/SBAS2 was tested for its antibody response using 3 groups of five Rhesus monkeys (RH). The first two groups, group 1 and 2 received RTS, S and gp120 (all undefined) with adjuvants SBAS2 or SB26T and were used as positive control. The **vaccine** Lipo D 1/3 Mage 3 His/SBA2 was administered to the right leg of group 3 RH at day 0, 28 and 84 by intramuscular injection at posterior part of leg. Small unheparinized blood samples of 3 ml were collected from femoral vein every 14 days and was allowed to clot for 1 hour. It was then centrifuged at 2500 rpm for 10 min. and serum was removed. The resulting contents were frozen at 20 deg. C and kinetics of antibody response was determined by ELISA. Result showed a clear boost in Mage 3 specific total antibody titre (no specific values given) in 3 out of 5 animals after second and third injection.
USE - The **vaccine** is used in medicine for immunotherapeutically treating patients suffering from melanomas or other MAGE associated tumors like breast, bladder, lung and non-small cell lung cancer, head and squamous cell carcinoma, colon carcinoma and esophagus carcinoma.
ADVANTAGE - The expression enhancer partners associated with the antigen increases the levels of protein expression. The derivatives like affinity tags helps in easier purification. Blocking agents used in the purification step prevents aggregation of product and therefore ensures stability for downward purification.
Dwg.0/19

L17 ANSWER 21 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-468944 [39] WPIDS
DNC C1999-137535
TI Solid nanospheres for genetic immunization of mammals, to raise immune response to antigen by cell-mediated and humoral immune responses.
DC A96 B04 **D16**
IN AUGUST, J T; LEONG, K W; TRUONG, V
PA (UYJO) UNIV JOHNS HOPKINS
CYC 85
PI WO 9936089 A1 19990722 (199939)* EN 33p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9921172 A 19990802 (199954)
EP 1045699 A1 20001025 (200055) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 9936089 A1 WO 1999-US860 19990115; AU 9921172 A AU 1999-21172 19990115;
EP 1045699 A1 EP 1999-901486 19990115, WO 1999-US860 19990115
FDT AU 9921172 A Based on WO 9936089; EP 1045699 A1 Based on WO 9936089
PRAI US 1998-71746 19980116
AB WO 9936089 A UPAB: 19990928

NOVELTY - New solid nanospheres of less than 5 mu m for genetic immunization of mammals comprising coacervate of polymeric cation and polyanion of nucleic acids, where at least a portion of the nucleic acids encode an antigen, and where a **cytokine** is encapsulated in coacervate.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) A method of immunizing a mammal to raise an immune response to an antigen comprising administering to a mammal a solid nanosphere as defined above; and

(2) a method of forming solid nanospheres for immunization of a mammal, comprising forming solid nanospheres by coacervation of a polyanion consisting of nucleic acids encoding an antigen and a polymeric cation, where the coacervation is done in the presence of a **cytokine** which is encapsulated in the solid spheres.

ACTIVITY - Antiviral; antibacterial; anti-tumor.

BALB/c mice (8 weeks) were divided into groups of 10. The mice were immunized by intramuscular injection in the tibialis anterior with three monthly injections of nanospheres containing 0.5 or 3 mu g nanosphere DNA encoding Ebola nucleoprotein (NP); 0.5 or 3 mu g nanosphere DNA encoding Ebola envelope glycoprotein (GP) antigens or 3 mu g control WRG7077 pDNA (vector without the Ebola NP or GP insert). The mice then were challenged with 30 multiply LD50 of mouse-adapted live Ebola Zaire strain. Survival rates were tabulated at week 12. No deaths were observed after day 10. The survival rate was better with each antigen than with vector control and was significantly greater with the higher dose (p less than 0.05). A higher degree of protection was achieved with Ebola NP vaccination than with Ebola GP (90% versus 40%). The geometric means anti-GP or anti-NP antibody titers of immunized mice were low, 1 plus or minus 0.1 multiply 102. Vaccination with DNA nanospheres was at least as efficient as the gene gun vaccination method. The results suggested that the nanosphere may provide an important new type of DNA **vaccine** delivery system of particular value in disease states in which a specific immune response phenotype is required. A parallel challenge experiment using the NP antigen given as PowerJect-XR (gene gun) gene gun DNA (3 mu g dose, three total vaccinations) showed a protection level of 80%.

MECHANISM OF ACTION - Cell mediated response stimulation; humoral immune response stimulation.

USE - The nanospheres are used to immunize mammals to raise immune response to antigen (claimed) by cell-mediated and humoral immune responses. They are also used to deliver genes encoding antigens to mammals, to target parenchymal cells of the liver sinusoids, fibroblasts of the connective tissues, cells in the Islets of Langerhans in the pancreas, cardiac myocytes, Chief and parietal cells of the intestine, osteocytes and chondrocytes in bone, keratinocytes, nerve cells of the peripheral nervous system, epithelial cells of the kidney and lung, Sertoli cells of the testis, erythrocytes, leukocytes (monocytes, macrophages, B and T lymphocytes, neutrophils, natural killer cells, progenitor cells, mast cells, eosinophils), platelets and endothelial cells. The nanospheres are used to immunize against HIV and Ebola infections.

ADVANTAGE - The nanosphere provides non-viral gene delivery system for delivery of nucleic acids for immunization of animals. Temporal and

spatial distribution of **cytokines** can be altered, thus directing immune response towards a specific immune arm, for example allowing modulating immune response against HIV infection by emphasizing humoral or cellular arm. Coacervate is extracellularly stable. Ligands can be conjugated to nanospheres to stimulate receptor-mediated endocytosis and potentially to target cells/tissues. Lysosomolytic agents can be incorporated to promote escape of intact DNA into cytoplasm. Other bioactive agents (RNA, oligonucleotides, proteins or multiple plasmids) can be co-encapsulated for potential augmentation of immune response through class I presentation. Bioavailability of nucleic acids is improved because of protection from serum nuclease degradation by the matrix and there is little release of nucleic acids until the nanosphere is sequestered into the endolysosomal pathway. There is potential of intracellular sustained release of nucleic acids that may provide more prolonged expression of gene product. Nanosphere is stable in plasma electrolytes and can be lyophilized without loss of bioactivity. Nanospheres can be handled like conventional pharmaceutical formulations in terms of production, reproducibility and storage.

DESCRIPTION OF DRAWING(S) - Survival of mice infected with Ebola virus following vaccination with Ebola nucleoprotein (NP) pDNA or Ebola envelope glycoprotein (GP) pDNA delivered by nanosphere. Open square = 0.5 mu g Ebola NP pDNA; filled square = 3 mu g Ebola NP pDNA; open circle = 0.5 mu g Ebola GP pDNA; filled circle = 3 mu g Ebola GP pDNA; open triangle = 3 mu g control WRG7077 pDNA (vector without the Ebola NP or GP insert).

5A, 5B/5

L17 ANSWER 22 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-243663 [20] WPIDS
DNC C1999-071033
TI Method for inducing a protective mucosal cytotoxic T lymphocyte immune response.
DC A96 B04 **D16**
IN BELYAKOV, I M; BERZOFSKY, J A; DERBY, M A; KELSALL, B L; STROBER, W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES; (USSH) US DEPT HEALTH & HUMAN SERVICE
CYC 83
PI WO 9912563 A2 19990318 (199920)* EN 85p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9893862 A 19990329 (199932)
EP 1011720 A2 20000628 (200035) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9912563 A2 WO 1998-US19028 19980911; AU 9893862 A AU 1998-93862 19980911; EP 1011720 A2 EP 1998-946965 19980911, WO 1998-US19028 19980911
FDT AU 9893862 A Based on WO 9912563; EP 1011720 A2 Based on WO 9912563
PRAI US 1998-74894 19980217; US 1997-58523 19970911
AB WO 9912563 A UPAB: 19990525
NOVELTY - A novel method for inducing a protective mucosal cytotoxic T lymphocyte (CTL) response in a mammalian subject comprises contacting a

mucosal tissue of the subject with a composition comprising a purified soluble antigen.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method for inducing a protective mucosal CTL response in a subject comprising contacting a mucosal tissue of the subject with a composition comprising a soluble antigen which does not comprise an adjuvant; and

(2) an immunogenic composition for inducing a protective mucosal CTL response in a subject and adapted for intrarectal administration comprising a purified soluble antigen formulated for intrarectal delivery to the rectum, colon, sigmoid colon or distal colon.

USE - The methods can induce a protective mucosal CTL response in a subject. The method can be used for protection against e.g. hepatitis A virus, papilloma virus, feline immunodeficiency virus, feline leukemia virus, Listeria monocytogenes, M. tuberculosis, M. leprae, or Giardia lamblia.

ADVANTAGE - The method induces long-lasting protective mucosal immune responses.

Dwg.0/17

L17 ANSWER 23 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-130421 [12] WPIDS
DNC C1998-043065
TI Immunogenic composition for treating cancer, e.g. leukaemia - comprises **tumour-associated antigen** and genetically engineered allogenic **cytokine**-expressing cells.
DC B04 **D16**
IN GRAF, M R; GRANGER, G A; HISERODT, J C
PA (REGC) UNIV CALIFORNIA
CYC 78
PI WO 9804282 A1 19980205 (199812)* EN 65p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9739655 A 19980220 (199828)
EP 915708 A1 19990519 (199924) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9804282 A1 WO 1997-US13205 19970725; AU 9739655 A AU 1997-39655 19970725; EP 915708 A1 EP 1997-937043 19970725, WO 1997-US13205 19970725
FDT AU 9739655 A Based on WO 9804282; EP 915708 A1 Based on WO 9804282
PRAI US 1997-901225 19970724; US 1996-23108 19960725; US 1996-29286 19961010
AB WO 9804282 A UPAB: 19980323
The following are claimed: (1) an immunogenic composition (A) for human administration comprising: (a) a **tumour-associated antigen** (TA-Ag) obtained from an autologous cell or its progeny, and (b) allogenic cells genetically engineered to produce a **cytokine** (I) at an elevated level; (2) a composition similar to (1), but where TA-Ag is replaced by autologous tumour cells or their progeny; (3) a composition similar to (1), but further comprising cells expressing a transmembrane (I) at a level that increases immune response to Ag; (4) brain cancer cells ACBT and their progeny, and (5) a method and kit for producing the above compositions.

USE - The compositions are used as **vaccines** to induce an antitumour response in a human, useful in treatment of neoplastic disease,
e.g. brain and ovarian cancers (all claimed), adenocarcinoma, lymphoma, leukaemia, melanoma, and sarcoma. The compositions are used after preliminary treatment by surgery, chemotherapy or radiation therapy, e.g. irradiating tumour cells with at least 5 krads of gamma -irradiation (claimed). Allogenic and primary tumour cells are each administered subcutaneously at 5-200x106, systemically at a site remote from the original tumour (claimed).

ADVANTAGE - **Vaccines** can be tailored for specific cancers or subjects, e.g. by altering (I) or the combination of (I). The (I)-producing cells act in trans to generate a specific response to Ag, at
both primary cancers and metastases, and provide a better response than tumour cells used alone or with adjuvants or co-factors. The (I)-producing
cells are prepared in advance and cloned to provide a consistent result and produce (I) even after inactivation, obviating the need to culture each autologous cell line. Since the autologous tumour cells will be HLA-compatible, they will persist at the site of injection.
Dwg.6/7

L17 ANSWER 24 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1997-514518 [48] WPIDS
DNC C1997-164499
TI Genetically modified CELO viruses - useful for gene therapy or **vaccine** production, e.g. against cancer.
DC B04 C06 **D16**
IN BAKER, A; CHIOCCA, S; COTTEN, M; KURZBAUER, R; SCHAFFNER, G
PA (BOEH) BOEHRINGER INGELHEIM INT GMBH
CYC 22
PI DE 19615803 A1 19971023 (199748)* 51p
WO 9740180 A1 19971030 (199749) DE 106p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP MX US
EP 904394 A1 19990331 (199917) DE
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2000509268 W 20000725 (200041) 139p
MX 9808653 A1 19990701 (200061)
ADT DE 19615803 A1 DE 1996-19615803 19960420; WO 9740180 A1 WO 1997-EP1944 19970418; EP 904394 A1 EP 1997-919383 19970418, WO 1997-EP1944 19970418; JP 2000509268 W JP 1997-537713 19970418, WO 1997-EP1944 19970418; MX 9808653 A1 MX 1998-8653 19981019
FDT EP 904394 A1 Based on WO 9740180; JP 2000509268 W Based on WO 9740180
PRAI DE 1996-19615803 19960420
AB DE 19615803 A UPAB: 19971222
The following are claimed: (1) a CELO (''chicken embryo lethal orphan'') virus obtainable by manipulation of CELO virus DNA in vitro; (2) CELO virus DNA contained in a plasmid which can replicate in bacteria or yeast and which provides virus particles after introduction into cells, optionally together with a plasmid that complements any gene necessary for
the production of mature virus particles that may be lacking in the CELO virus; and (3) helper cells (especially avian cells) containing CELO virus
genes integrated into their genome.

USE - Modified CELO viruses containing exogenous DNA encoding a therapeutic protein are useful for gene therapy. Modified CELO viruses containing exogenous DNA encoding an immunostimulant protein (especially a **cytokine**) or a **tumour-associated antigen** or **antigen** fragment can be used to produce cancer **vaccines**. Modified CELO viruses containing exogenous DNA encoding an antigen derived from a human, animal or avian pathogen can be used to produce **vaccines** against infectious diseases of humans, animals and birds, respectively.
Dwg.0/7

L17 ANSWER 25 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1997-350783 [32] WPIDS
DNC C1997-113248
TI Inducing humoral and cellular immune response against tumour antigens or infectious agents - by intradermal then intravenous administration of immunoconjugate comprising antibody against HLA-DR complex and antigenic peptide, optionally boosted with **cytokine** or additional antibody.
DC B04 **D16**
IN HANSEN, H J
PA (IMMU-N) IMMUNOMEDICS INC
CYC 75
PI WO 9723237 A1 19970703 (199732)* EN 51p
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9712871 A 19970717 (199745)
EP 881910 A1 19981209 (199902) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2000503003 W 20000314 (200024) 46p
AU 721927 B 20000720 (200040)
ADT WO 9723237 A1 WO 1996-US19755 19961220; AU 9712871 A AU 1997-12871 19961220; EP 881910 A1 EP 1996-943706 19961220, WO 1996-US19755 19961220; JP 2000503003 W WO 1996-US19755 19961220, JP 1997-523703 19961220; AU 721927 B AU 1997-12871 19961220
FDT AU 9712871 A Based on WO 9723237; EP 881910 A1 Based on WO 9723237; JP 2000503003 W Based on WO 9723237; AU 721927 B Previous Publ. AU 9712871, Based on WO 9723237
PRAI US 1995-577106 19951222
AB WO 9723237 A UPAB: 19970806
Humoral and cellular immune responses are induced in mammals against: (i) a tumour that expresses a **tumour-associated antigen** (TAA); or (ii) an infectious agent by: (a) intradermal administration of a **vaccine** (A) comprising an immunoconjugate (I) consisting of an antibody component (II) that binds to the HLA-DR complex and an antigenic peptide (III) containing at least 1 epitope of TAA or an antigen associated with the infectious agent; and (b) intravenous administration of (A). Also new are: (1) a similar method for generating response against TAA in which the antigenic peptide (IIIa) induces a major histocompatibility complex (MHC)-restricted response; and (2) generating responses against a tumour that expresses carcinoembryonal antigen (CEA) by administration of: (a) **vaccine** containing antibody component that binds CEA, coupled to a soluble immunogenic

carrier protein (SICP); (b) **vaccine** containing anti-idiotype antibody that mimics a CEA epitope (also coupled to SICP); and (c) vac cine comprising (I) made of (III) containing a CEA epitope and (II).

USE - The method is used to treat tumours and to prevent infection by e.g. viruses, bacteria and protozoa. The dose of (I) and antibodies is 1 pg-10 mg/kg, and a typical dose of **cytokine** is 0.6 million units/kg interleukin (IL)-2 intravenously or 12 million units subcutaneously.

ADVANTAGE - The method produces an integrated response and this can be enhanced by administration of additional antibodies or **cytokines** (to amplify cytotoxic T cells induced by the initial intradermal injection).

Dwg.0/0

L17 ANSWER 26 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1997-331550 [30] WPIDS
CR 1993-134149 [16]; 1997-087021 [08]
DNC C1997-106376
TI Treatment of tumours by stimulation of immune response - comprises administering irradiated tumour cells expressing **granulocyte-macrophage colony-stimulating factor**
.
DC B04 D16
IN DRANOFF, G; MULLIGAN, R C; PARDOLL, D
PA (UYJO) UNIV JOHNS HOPKINS SCHOOL MEDICINE; (WHED) WHITEHEAD INST BIOMEDICAL RES
CYC 1
PI US 5637483 A 19970610 (199730)* 29p
ADT US 5637483 A CIP of US 1991-771194 19911004, Cont of US 1992-956621 19921005, US 1994-265554 19940623
PRAI US 1992-956621 19921005; US 1991-771194 19911004; US 1994-265554 19940623
AB US 5637483 A UPAB: 19990714
Stimulation of immune response to tumour in a mammal comprises administering tumour cells that have been rendered **proliferation -incompetent** by irradiation and have been genetically engineered to express **granulocyte-macrophage colony-stimulating factor (GM-CSF)**, provided that the tumour and the tumour cells are of the same type.

USE -The invention is for treating melanoma or carcinomas, especially carcinoma of the lung, kidney, colon, breast or prostate. The invention provides for the regulation, either in a stimulatory or suppressive way, of an individuals immune response to an antigen. The invention is used to reverse or suppress as well as to prevent disease, it is used to protect an individual against the development or progression of a tumour, bacterial or viral infection such as AIDS, rejection of transplanted tissue, or autoimmune condition. In addition, the invention may be useful in the treatment of chronic and life threatening infections, e.g. the secondary infections associated with AIDS, as well as other bacterial, fungal, viral, parasitic and protozoal infections. A tumour cell of the type against which an enhanced immune response is desired can be engineered to express the cytokines to be administered. The resulting genetically engineered tumour cell is used as a **vaccine**, to protect against future tumour development or as a delivery vehicle to result in the reversal of previously existing tumours.

ADVANTAGE - Cytokines may be selected to optimise effects in the individual and thus maximise the desired result.
Dwg.0/9

L17 ANSWER 27 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-057704 [06] WPIDS
DNC C1996-019148
TI Breast cancer **vaccine**, developing lymphocyte immunity - contg. **tumour associated antigen** and low, non-toxic doses of **granulocyte-macrophage colony stimulating factor** and interleukin-2.
DC B04 **D16**
IN ELLIOTT, R L; HEAD, J F
PA (ELLI-I) ELLIOTT R L; (HEAD-I) HEAD J F
CYC 1
PI US 5478556 A 19951226 (199606)* 8p
ADT US 5478556 A US 1994-202516 19940228
PRAI US 1994-202516 19940228
AB US 5478556 A UPAB: 19960212
A compsn. comprises 0.1 ml of a suspension contg. a human breast cancer **tumour associated antigen** (TAA), 1,000,000 CFU of **granulocyte-macrophage colony stimulating factor** (**GM-CSF**) and 10,000 IU of interleukin-2 (IL-2). Also claimed is a breast tumour **vaccine** comprising a suspension of a TAA from a human breast tumour, 1,000,000 CFU of **GM-CSF** and 10,000 IU of IL-2, pref. in a vol. of ca. 0.3 ml.
USE - The **vaccine** is used in a cancer vaccination process, involving priming the patient's immune system with a chemotherapeutic antineoplastic agent (e.g. cisplatin-transferrin) prior to vaccination, to stimulate lymphocyte proliferation; administering the **vaccine** (pref. intradermally into the groin area, where inguinal and mesentery lymph node drainage promotes infiltration of lymphocytes and monocytes into the injection site; and administering an oral lymphocyte proliferative stimulator (e.g. the antidepressant fluoxetine) simultaneously with and after the vaccination. The developed lymphocyte immunity against TAA is useful in growth control or eradication of occult or evident metastatic cancer cells.
ADVANTAGE - The combination of agents optimises potential development of lymphocyte immunity against tumours. **GM-CSF** stimulates monocytes (vital in antigen processing and antigen presentation to lymphocytes); and IL-2 stimulates clonal expansion of T-lymphocytes. There are no toxicity problems, since IL-2 and **GM-CSF** are used at low doses, with only three weekly injections.
Dwg.0/3

L17 ANSWER 28 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-263767 [32] WPIDS
CR 1983-707055 [28]; 1988-056484 [08]; 1989-130047 [17]; 1990-305017 [40]; 1990-348485 [46]; 1992-096889 [12]; 1992-175125 [21]; 1992-200174 [24]; 1992-268664 [32]; 1992-331718 [40]; 1992-349203 [42]; 1993-018128 [02]; 1993-026900 [03]; 1993-076502 [09]; 1993-243234 [30]; 1995-036113 [05]; 1995-366231 [47]; 1995-366385 [47]; 1996-187644 [19]; 1997-042857 [04]; 1997-043114 [04]; 1997-051904 [05]; 1998-321465 [28]; 1998-332054 [29];

1998-332055 [29]; 1998-332145 [29]; 1999-493494 [41]; 1999-610231 [52]; 2001-280989 [27]

DNC C1994-120658

TI Attenuated recombinant virus used for cancer therapy - comprises DNA encoding **cytokine** and/or **tumour associated antigen**.

DC B04 **D16**

IN COX, W I; PAOLETTI, E; TARTAGLIA, J; PAOLETTI, E D

PA (VIRO-N) VIROGENETICS CORP

CYC 21

PI WO 9416716 A1 19940804 (199432)* EN 232p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9461652 A 19940815 (199444)
EP 680331 A1 19951108 (199549) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 09503902 W 19970422 (199726) 225p
AU 684070 B 19971204 (199806)
AU 9856457 A 19980604 (199839)
EP 680331 A4 19971203 (199840)
US 5833975 A 19981110 (199901)
AU 719456 B 20000511 (200031)

ADT WO 9416716 A1 WO 1994-US888 19940121; AU 9461652 A AU 1994-61652 19940121;
EP 680331 A1 EP 1994-908635 19940121, WO 1994-US888 19940121; JP 09503902 W JP 1994-517281 19940121, WO 1994-US888 19940121; AU 684070 B Add to AU 1992-15871 19920309, AU 1994-61652 19940121; AU 9856457 A Div ex AU 1994-61652 19940121, AU 1998-56457 19980304; EP 680331 A4 EP 1994-908635 19940121; US 5833975 A CIP of US 1989-320471 19890308, Div ex US 1990-478179 19900214, CIP of US 1991-638080 19910107, CIP of US 1991-666056 19910307, CIP of US 1991-713967 19910611, CIP of US 1991-805567 19911216, CIP of US 1992-847977 19920303, CIP of US 1992-847951 19920306, CIP of US 1993-7115 19930121, US 1994-184009 19940119; AU 719456 B Div ex AU 1994-61652 19940121, AU 1998-56457 19980304

FDT AU 9461652 A Based on WO 9416716; EP 680331 A1 Based on WO 9416716; JP 09503902 W Based on WO 9416716; AU 684070 B Previous Publ. AU 9461652, Based on WO 9416716; US 5833975 A CIP of US 5155020; AU 719456 B Div ex AU 684070, Previous Publ. AU 9856457

PRAI US 1994-184009 19940119; US 1993-7115 19930121; US 1989-320471 19890308; US 1990-478179 19900214; US 1991-638080 19910107; US 1991-666056 19910307; US 1991-713967 19910611; US 1991-805567 19911216; US 1992-847977 19920303; US 1992-847951 19920306

AB WO 9416716 A UPAB: 20010528
A modified recombinant virus (A) has virus-encoded genetic functions inactivated, resulting in attenuated virulence but retained efficacy, and further comprises exogenous DNA in a non essential region of the virus genome, encoding >1 **cytokine** and/or **tumour associated antigen** (TAA). Also claimed are: (1) a method for expressing a gene prod. in a cell cultured in vitro, comprising introducing into the cell the virus; and (2) a **cytokine** and/or TAA prepared from in vitro expression of the virus.

The virus is pref. a MYVAC or ALVAC recombinant virus and the exogenous DNA pref. encodes 1 of: human TNF, nuclear phosphoprotein p53, wild type or mutant, human melanoma-associated Ag, IL-2, IFN-gamma, IL-4, **GM-CSF**, IL-12, 37, erb-B-2 or carcino embryonic Ag.

USE - The virus is useful, in a compsn. (claimed), for inducing an antigenic or immunological response, i.e. for immunisation against pathogens. It can be specifically used for treating patients in need of cancer treatment.

In an example, ALVAC-RG (VCP65) was generated and grown in primary CEF for scaling up. The vaccinia virus suspension was obtained by ultrasonic disruption in serum free medium of infected cells. Cell debris was removed and the resulting suspension was supplemented by lyophilisation stabiliser, dispensed in simple dose vials and freeze dried. Healthy adults (25) with no previous history of rabies immunisation were randomly allocated to receive standard human diploid cell rabies **vaccine** (HDC) or the shdy **vaccine**, ALVAC-RG (VCP65). Three batches of VCP65 **vaccine** were used sequentially in 3 groups of volunteers (A, B and C), with 2 week intervals between each step. The conc. of batches was 10 3.5, 10 4.5 and 10 5.5 TCID50/dose. Each volunteer received 2 doses of the same **vaccine** s.c. at a 4 week interval. Six months later the recipients of the highest dose of v.CP65 (group C) and HDC **vaccine** were offered a 3rd dose of **vaccine**. They were then randomised to receive the same or the alternate **vaccine**. Four groups were thus formed: (1) HDC, HDC-HDC; (2) HDC, HDC-vCP65; (3) vCP65, vCP65-HDC; (4) vCP65, vCP65-vCP65.

Antibody (Ab) assays were carried out. The non-replicating pox virus vCP65 was shown to be an effective immunising vector in humans, without the safety problem created by a fully permissive virus. The booster chase resulted in further increase in rabies Ab titres.

Dwg.0/39

L17 ANSWER 29 OF 29 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-150931 [18] WPIDS
DNC C1994-069347
TI New immuno-complex of lymphoma associated antigen and **cytokine** - for protection against B cell lymphoma proliferation, also related nucleic acid, recombinant cells antibodies, etc..
DC B04 **D16**
IN LEVY, R; TAO, M
PA (STRD) UNIV LELAND STANFORD JUNIOR
CYC 46
PI WO 9408601 A1 19940428 (199418)* EN 33p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR BY CA CH CZ DE DK ES FI GB HU JP KP KR KZ LK LU LV MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US UZ VN
AU 9453617 A 19940509 (199432)
US 6099846 A 20000808 (200040)
ADT WO 9408601 A1 WO 1993-US9895 19931014; AU 9453617 A AU 1994-53617 19931014; US 6099846 A CIP of US 1992-961788 19921014, WO 1993-US9895 19931014, US 1995-416787 19950414
FDT AU 9453617 A Based on WO 9408601; US 6099846 A Based on WO 9408601
PRAI US 1992-961788 19921014; US 1995-416787 19950414
AB WO 9408601 A UPAB: 19940622
New immunocomplex (A) consists of a B-cell lymphoma **tumour-associated antigen** (Ag), or epitope-bearing part of it, covalently bound to an immune-enhancing **cytokine** (I). Also new

are (1) DNA encoding (A); (2) recombinant expression system for producing (A) as a fusion protein (3) recombinant host cells transferred with this expression system, (4) antibodies reactive with the epitope-bearing part of (A) or immunospecific for (A); (5) any conjugate (A') consisting of (I) covalently bonded to an additional molecular structure. Pref. Ag is an immunoglobulin (Ig) and the epitope-bearing part is the idiotypic region of this Ig.

USE - (A) is useful in **vaccines** to protect against proliferation of B cell lymphoma, while the antibodies can be used to confer passive resistance to such proliferation.

Dwg.5/8

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FROM JANUARY 1969 TO DATE.

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L1          4404 S TUMOR (2A) ASSOC? (3A) ANTIGEN#
L2             3 S PROLIFERATION INCOMP?
L3             0 S L1 AND L2
L4         10496 S GM CSF OR GRANULOCYTE? STIMUL? FACTOR#
L5            37 S L1 AND L4
L6        102822 S VACCINE# OR ANTITUMOR OR ANTICANCER#
L7             0 S L5 AND L
L8            19 S L5 AND L6
L9        138150 S VACCIN? OR IMMUNIZ?
L10           21 S L5 AND L9
L11           24 S L10 OR L8

     FILE 'BIOSIS' ENTERED AT 13:26:24 ON 06 AUG 2001

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L11  ANSWER 1 OF 24  BIOSIS  COPYRIGHT 2001 BIOSIS
AN   2001:317607  BIOSIS
DN   PREV200100317607
TI   Dendritic cell therapy of glioblastoma: Evidence of antitumor
     immune response in vivo.
AU   Chuhjo, Tatsuya (1); Wang, Hongbo (1); Kondo, Yukio (1); Uchiyama,
     Naoyuki; Hayashi, Yutaka; Fujii, Shin-ichiro; Yamashita, Sumihiro; Nakao,
     Shinji (1)
CS   (1) Third Department of Medicine, Kanazawa University School of medicine,
     Kanazawa, Ishikawa Japan
SO   Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 617a. print.
     Meeting Info.: 42nd Annual Meeting of the American Society of Hematology
     San Francisco, California, USA December 01-05, 2000 American Society of
     Hematology
     . ISSN: 0006-4971.
DT   Conference
LA   English
SL   English
AB   Vaccination with antigen pulsed dendritic cells (DC) has been
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applied to various malignancies with the hope of eliciting anti-tumor immunity in vivo. Glioblastoma, a representative malignancy resistant to chemoradiotherapy, is known to express several **tumor-associated antigens** and may therefore be a good target of DC therapy. We treated two patients (patients 1 and 2) with refractory glioblastoma using antigen-pulsed DC. Both patients had unresectable glioblastoma of the cerebrum and had been treated with irradiation with no response before **vaccination**. DC were induced from peripheral blood progenitor cells mobilized with G-CSF by the culture in the presence of **GM-CSF**, IL-4 and TNFalpha for 11 days. In patient 1, DC were pulsed with a lysate of the tumor cells on the fifth day of the culture. A total of 106 DC were injected intravenously three times every two weeks. Immature DC were pulsed with apoptotic tumor cells derived from autologous glioblastoma cell line on the fifth day of culture for patient 2. A total of 106 DC were injected intradermaly every three weeks for six times. Delayed type hypersensitivity (DTH) reaction to the injected tumor lysate developed around the last DC injection in patient 1. The primary tumor lesion in the left hemisphere of the patient regressed at 4 months after DC therapy but the secondary lesion in the right hemisphere continued to grow, and the patient died of brain tumor. Patient 2 failed to show DTH reaction to a tumor lysate but the tumor regressed and remained in PR for 6 months after **vaccination**. Cytotoxic activity to autologous tumor cells was induced in peripheral blood T cells of patient 2. Either patient did not show any adverse effect associated with DC injections. In both patients, tumors biopsied before **vaccination** showed only sparse infiltration of lymphocyte. Autopsy of patient 1 and biopsy of patient 2 after **vaccination** showed dense infiltration of CD3+ CD8+ CD45RO+ T lymphocytes to residual tumors but not to the normal brain tissue. This is the first report of successful DC therapy for glioblastoma. The results show that **vaccination** with tumor antigen-pulsed DC can elicit immune response to glioblastoma in vivo and warrant further investigation.

IT Major Concepts
Oncology (Human Medicine, Medical Sciences)

IT Diseases
glioblastoma: immunotherapy, neoplastic disease, nervous system disease

IT Alternate Indexing
Glioblastoma (MeSH)

IT Methods & Equipment
dendritic cell therapy: in-vivo **antitumor** response evidence, therapeutic method

IT Miscellaneous Descriptors
Meeting Abstract; Meeting Poster

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): patient

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L11 ANSWER 2 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:309049 BIOSIS
DN PREV200100309049
TI Recruitment of dendritic cells and enhanced antigen-specific immune reactivity in cancer patients treated with hr-**GM-CSF** (Molgramostim) and hr-IL-2: Results from a phase Ib clinical trial.
AU Correale, P.; Campoccia, G.; Tsang, K. Y.; Micheli, L.; Cusi, M. G.; Sabatino, M.; Bruni, G.; Sestini, S.; Petrioli, R.; Pozzessere, D.; Marsili, S.; Fanetti, G.; Giorgi, G.; Francini, G. (1)
CS (1) Division of Medical Oncology, University of Siena, Viale Bracci 11, 53100, Siena: francini@unisi.it Italy
SO European Journal of Cancer, (May, 2001) Vol. 37, No. 7, pp. 892-902. print.
ISSN: 0959-8049.
DT Article
LA English
SL English
AB Experimental findings suggest that granulocyte-monocyte-colony stimulating factor (**GM-CSF**) synergistically interacts with interleukin-2 (IL-2) in generating an efficient antigen-specific immune response. We evaluated the toxicity, antitumour activity and immunobiological effects of human recombinant (hr)-**GM-CSF** and hr-IL-2 in 25 cancer patients who subcutaneously (s.c.) received hr-**GM-CSF** 150 mug/day for 5 days, followed by hrIL-2 s.c. for 10 days and 15 days rest. Two of the most common side-effects were bone pain and fever. Of the 24 patients evaluable for response, 3 achieved partial remission, 13 experienced stable disease, and 8 progressed. Cytokine treatment increased the number of monocytes, dendritic cells (DC), and lymphocytes (memory T cells) in the peripheral blood and enhanced the antigen-specific immunoreactivity of these patients. Our results show that the hr-**GM-CSF** and hr-IL-2 combination is active and well tolerated. Its biological activity may support tumour associated antigen (TAA)-specific **anticancer** immunotherapy by increasing antigen presenting cell (APC) activity and T cell immune competence in vivo.
IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Pharmacology
IT Parts, Structures, & Systems of Organisms
T cell: blood and lymphatics, immune system; antigen presenting cell: immune system; dendritic cells: immune system; lymphocytes: blood and lymphatics, immune system; monocytes: blood and lymphatics, immune system
IT Diseases
cancer: neoplastic disease
IT Chemicals & Biochemicals
human recombinant-granulocyte-monocyte-colony stimulating factor-human recombinant-interleukin-2: antineoplastic - drug, immunologic - drug, side-effects, subcutaneous administration, toxicity; **tumor associated antigen**
IT Alternate Indexing
Neoplasms (MeSH)
IT Miscellaneous Descriptors

antigen-specific immune reactivity
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L11 ANSWER 3 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:291233 BIOSIS
DN PREV200100291233
TI HLA-A*0201 binding affinity of peptides derived from p53, CEA, HER2/neu and MAGE2/3 correlates with immunogenicity and epitope presentation by tumor cell lines.
AU Keogh, Elissa (1); Fikes, John (1); Southwood, Scott (1); Sette, Alessandro (1)
CS (1) Epimmune Inc., 5820 Nancy Ridge Drive, San Diego, CA, 92121 USA
SO FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A321. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DT Conference
LA English
SL English
AB The relationship between MHC binding affinity and immunogenicity of class I-restricted, infectious disease-derived epitopes is well established, with high affinity binding strongly correlating with immunogenicity in humans. However, the extent to which this correlation applies to "self"-derived **tumor-associated antigens** (TAA) remains controversial. In this study, we have tested 34 wild-type and analog peptides derived from p53, CEA, HER2/neu and MAGE2/3 for their capacity to induce cytotoxic T lymphocytes (CTL) in vitro that are capable of recognizing tumor target lines. All the peptides bound HLA-A*0201 and at least 2 additional A2 supertype alleles with an IC50 &61603; 500 nM. Twenty of 22 wild-type and 9 of 12 single-substitution analogs were found to be immunogenic in primary in vitro human CTL inductions with normal PBMC and **GM-CSF**/IL4-induced dendritic cells (DC) from HLA-A*0201 individuals, when tested on wild-type peptide-pulsed target cells. Recognition of naturally-processed antigen presented by tumor cell lines was noted for 19 of 35 peptides, with recognition associated with strong HLA-A*0201 binding (IC50 200 nM or less; P = 0.008). These data demonstrate that CTL precursors specific for high affinity, TAA-derived epitopes exist in the human T cell repertoire, and that these CTL are of sufficient avidity to recognize tumor cells expressing the naturally-processed antigen. The implications of these findings for the development of epitope-based cancer **vaccines** will be discussed.ltoreq
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Tumor Biology
IT Parts, Structures, & Systems of Organisms
T cell: blood and lymphatics, immune system, repertoire; cytotoxic T lymphocyte [CTL]: blood and lymphatics, immune system
IT Chemicals & Biochemicals
CEA [carcinoembryonic antigen]; HER2/neu; HLA-A: binding affinity; MAGE2/3; MHC [major histocompatibility complex]: binding affinity;

naturally-processed antigen; p53; **tumor-associated antigens**: self-derived
IT Miscellaneous Descriptors
epitope presentation; immunogenicity; tumor cell lines; Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L11 ANSWER 4 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:181538 BIOSIS
DN PREV200100181538
TI Enhancement of B cell lymphoma and tumor resistance using idiotype/cytokine conjugates.
AU Levy, Ronald (1); Tao, Mi-Hua
CS (1) Stanford, CA USA
ASSIGNEE: The Board of Trustees of the Leland Stanford Junior University
PI US 6099846 August 08, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents,
(Aug. 8, 2000) Vol. 1237, No. 2, pp. No Pagination. e-file.
ISSN: 0098-1133.
DT Patent
LA English
AB B cell lymphoma **tumor-associated antigen** or a fragment thereof containing an epitope are linked to an immune-enhancing
cytokine, such as **GM-CSF**, IL-2, or IL-4 to form an immuno-complex. This immuno-complex elicits immune responses which are protective with respect to tumor proliferation. The linkers may be simple chemical bifunctional moieties introduced through chemical synthetic techniques or peptides introduce through recombinant methodologies. Antibodies immunoreactive with these immunocomplexes are also useful as passive **vaccines** and as analytical tools.
IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences); Oncology (Human
Medicine, Medical Sciences); Pharmacology
IT Diseases
B cell lymphoma: blood and lymphatic disease, immune system disease, neoplastic disease
IT Chemicals & Biochemicals
B cell lymphoma **antitumor vaccine: vaccine**
IT Alternate Indexing
Lymphoma, B-Cell (MeSH)

L11 ANSWER 5 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:68974 BIOSIS
DN PREV200100068974
TI Peptide **vaccination** in clinical oncology.
AU Jaeger, E.; Jaeger, D.; Knuth, A. (1)
CS (1) II. Medizinische Klinik, Haematologie - Onkologie, Krankenhaus Nordwest, Steinbacher Hohl 2-26, D-60488, Frankfurt/M. Germany
SO Onkologie, (Oktober, 2000) Vol. 23, No. 5, pp. 410-415. print.

ISSN: 0378-584X.
DT General Review
LA English
SL English; German
AB **Tumor-associated antigens** recognized by cellular or humoral effectors of the immune system represent attractive targets for antigen-specific cancer therapy. Different groups of cancer-associated antigens have been identified inducing cytotoxic T-lymphocyte (CTL) responses in vitro and in vivo: 1) 'Cancer-Testis' (CT) antigens, which are expressed in different tumors and normal testis, 2) melanocyte differentiation antigens, 3) point mutations of normal genes, 4) antigens that are overexpressed in malignant tissues, and 5) viral antigens. Clinical studies with peptides derived from these antigens have been initiated to study the induction of specific CTL responses in vivo. Immunological and clinical parameters for the assessment of peptide-specific reactions have been defined, i.e., delayed-type hypersensitivity (DTH), CTL, autoimmune, and tumor regression responses. Early results show that tumor-associated peptides alone induce specific DTH and CTL responses and tumor regression after intradermal administration. **GM-CSF** was used as an adjuvant to enhance peptide-specific immune reactions by amplification of dermal peptide-presenting dendritic cells. Complete tumor regressions have been observed in the context of measurable peptide-specific CTL. However, in single cases with disease progression after an initial tumor response, either a loss of the respective tumor antigen targeted by CTL or of the presenting MHC class I allele was detected, suggesting **immunization**-induced immune escape. Based on these observations, cytokines to modify antigen and MHC class I expression in vivo are being tested to prevent immunoselection. Recently, a new CT antigen, NY-ESO-1, has been identified with a strategy utilizing spontaneous antibody responses to **tumor-associated antigens** (SEREX). NY-ESO-1 is regarded as one of the most immunogenic antigens known today, inducing spontaneous immune responses in 50% of patients with NY-ESO-1-expressing cancers. Clinical studies with antigenic constructs to induce both humoral and cellular immune responses will show whether these are more effective for immunotherapy of cancer.
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Tumor Biology
IT Parts, Structures, & Systems of Organisms
cytotoxic T lymphocytes: blood and lymphatics, immune system; melanocytes: differentiation, integumentary system; testis: reproductive system
IT Chemicals & Biochemicals
MHC class I [major histocompatibility complex class I]: expression; NY-ESO-1: cancer-testis antigen, expression, immunogenic; cancer-testis antigens; **tumor-associated antigens**
IT Methods & Equipment
immunotherapy: therapeutic method; peptide **vaccination**: **immunization** method, therapeutic method
IT Miscellaneous Descriptors
cellular immune response; humoral immune response; tumor regression
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L11 ANSWER 6 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:31281 BIOSIS
DN PREV200100031281
TI **Vaccination** with a mixed **vaccine** of autogenous and allogeneic breast cancer cells and **tumor associated antigens** CA15-3, CEA and CA125: Results in immune and clinical responses in breast cancer patients.
AU Jiang, Xian Peng; Yang, Ding C.; Elliott, Robert L.; Head, Jonathan F. (1)
CS (1) Mastology Research Institute, 8221 Kelwood Avenue, Baton Rouge, LA, 70806: emcmri@iamerica.net USA
SO Cancer Biotherapy & Radiopharmaceuticals, (2000) Vol. 15, No. 5, pp. 495-505. print.
ISSN: 1084-9785.
DT Article
LA English
SL English
AB In breast cancer there is often overexpression of the breast cancer antigen CA15-3, the carcinoembryonic antigen (CEA) and the ovarian cancer antigen CA125, which makes them potential target antigens for immunotherapy. In this study, we used a multi-antigen **vaccine**, which included the following antigens: autologous breast cancer cells (AUTOC), allogeneic breast cancer MCF-7 cells (ALLOC), and the **tumor associated antigens** CA15-3, CEA and CA125, plus low doses of granulocyte/macrophage-colony-stimulating factor (**GM-CSF**) and interleukin 2 (IL-2). Forty-two breast cancer patients received weekly subcutaneous **vaccination** at the 1st, 2nd, 3rd, 7th, 11th and 15th weeks. Their lymphocyte proliferative responses to AUTOC, ALLOC, CA15-3, CEA and CA125 were tested in lymphocyte blastogenesis assays (LBA) before and after **vaccination**. The disease stage and serum CA15-3, CEA and CA125 concentrations were also determined pre- and post-**vaccination**. We found that the **vaccine** was safe, and the only major side effects were swelling at the site of injection, muscle pain, and weakness or fatigue. The **vaccine** induced a significant increase in post-**vaccination** lymphocyte proliferative responses to AUTOC, CA15-3, CEA and CA125 but not ALLOC, compared to pre-**vaccination** ($p<0.05$, $p<0.01$, $p<0.05$, $p<0.01$ and $p>0.05$, respectively, a paired t Test). Computed tomography (CT), ultrasound or bone scan showed evidence of disease improvement in 2 (12%) patients after **vaccination**. Hepatic metastases were reduced in size and number and some actually disappeared one patient. Metastatic disease in the L5 vertebra and the skull decreased in size and some osteolytic sites completely healed in a second patient. In addition, 7 patients (44%) had stable disease and 7 patients (44%) had disease progression. We did not find **vaccination** significantly reduced serum tumor markers CA15-3, CEA and CA125 of these breast cancer patients.
These results suggest that the **vaccine** mixture of autologous and allogeneic breast cancer cells and **tumor associated antigens** plus **GM-CSF** and IL-2 can be

administered safely to breast cancer patients and there is evidence for improved immunity and clinical efficacy.
IT Major Concepts
Oncology (Human Medicine, Medical Sciences)
IT Diseases
breast cancer: immunotherapy, neoplastic disease, reproductive system disease/female
IT Alternate Indexing
Breast Neoplasms (MeSH)
IT Methods & Equipment
mixed **vaccine** treatment: allogeneic tumor cells, autogenous tumor cells, cancer antigen 125, cancer antigen 15-3, carcinoembryonic antigen, clinical response, immune response, therapeutic method
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): female, patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L11 ANSWER 7 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:392237 BIOSIS
DN PREV200000392237
TI Cancer immunotherapy in clinical oncology.
AU Knuth, Alexander (1); Jaeger, Dirk; Jaeger, Elke
CS (1) Haematologie-Onkologie, II Medizinische Klinik, Steinbacher Hohl 2-26,
Krankenhaus Nordwest, 60488, Frankfurt am Main Germany
SO Cancer Chemotherapy and Pharmacology, (June, 2000) Vol. 46, No. Supplement, pp. S46-S51. print.
ISSN: 0344-5704.
DT General Review
LA English
SL English
AB The identification of **tumor-associated antigens** recognized by cellular or humoral effectors of the immune system has opened new perspectives for cancer therapy. Different groups of
cancer-associated antigens have been described as targets for cytotoxic T lymphocytes (CTLs) in vitro and in vivo: 1) cancer-testis (CT) antigens, which are expressed in different tumors and normal testis; 2) melanocyte differentiation antigens; 3) point mutations of normal genes; 4) antigens that are overexpressed in malignant tissues; and 5) viral antigens. Clinical studies with peptides derived from these antigens have been initiated to induce specific CTL responses in vivo. Immunological and clinical parameters for the assessment of peptide-specific reactions have been defined, i.e., delayed-type hypersensitivity (DTH), CTL, autoimmune, and tumor regression responses. Preliminary results demonstrate that tumor-associated peptides alone elicit specific DTH and CTL responses leading to tumor regression after intradermal injection. Granulocyte-macrophage colony-stimulating factor (**GM-CSF**) was proven effective in enhancing peptide-specific immune reactions by amplification of dermal peptide-presenting dendritic cells. Long-lasting complete tumor regressions have been observed after induction of peptide-specific CTLs. However, in single cases with disease progression after an initial tumor response, either a loss of the respective tumor antigen targeted by CTLs or of the presenting major histocompatibility

complex (MHC) class I allele was detected as a mechanism of immune escape under **immunization**. Based on these observations, cytokines to enhance antigen and MHC class I expression in vivo are being evaluated to prevent immunoselection. Recently, a strategy utilizing spontaneous antibody responses to **tumor-associated antigens** (SEREX) has led to the identification of a new CT antigen, NY-ESO-1, which is regarded as one of the most immunogenic antigens known today inducing spontaneous immune responses in 50% of patients with NY-ESO-1-expressing cancers. Clinical studies involving antigenic constructs that induce both antibody and CTL responses will show whether these are more effective for immunotherapy of cancer.

IT Major Concepts
Oncology (Human Medicine, Medical Sciences)

IT Diseases
melanoma: immunotherapy, neoplastic disease; renal cell carcinoma: immunotherapy, neoplastic disease, urologic disease

IT Chemicals & Biochemicals
cancer-testis antigen: cancer immunotherapy use, immune system recognition; melanocyte differentiation antigen: cancer immunotherapy use, immune system recognition

IT Alternate Indexing
Melanoma (MeSH); Kidney Neoplasms (MeSH); Carcinoma, Renal Cell (MeSH)

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): patient

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L11 ANSWER 8 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:369758 BIOSIS
DN PREV200000369758
TI Feeding dendritic cells with tumor antigens: Self-service buffet or a la carte.
AU Melero, I. (1); Vile, R. G.; Colombo, M. P.
CS (1) Department of Medicine, School of Medicine, University of Navarra, C/Irunlarrea, 1, 31008, Pamplona Spain
SO Gene Therapy, (July, 2000) Vol. 7, No. 14, pp. 1167-1170. print. ISSN: 0969-7128.
DT Article
LA English
SL English
AB Adoptive transfer of autologous dendritic cells (DC) presenting **tumor-associated antigens** initiate and sustain an immune response which eradicate murine malignancies. Based on these observations, several clinical trials are in progress testing safety and efficacy with encouraging preliminary reports. In these approaches, ex vivo incubation of DC with a source of tumor antigens is required to load the relevant antigenic epitopes on the adequate antigen presenting molecules. Recent data show that in some instances exogenous DC artificially injected into malignant tissue or endogenous DC attracted to the tumor nodule by means of gene transfer of **GM-CSF** and CD40L into malignant cells result in efficacious **antitumor** immunity. In the case of intratumoral injection of DC the procedure is curative only if DC had been genetically engineered to produce IL-12, IL-6

or to express CD40L. Evidence has been obtained showing that intratumoral DC can capture and process tumor antigens to be presented to T-lymphocytes. Although the exact mechanisms of tumor antigen acquisition by DC are still unclear, available data suggest a role for heat shock proteins released from dying malignant cells and for the internalization of tumor-derived apoptotic bodies. Roles for tumor necrosis versus apoptosis are discussed in light of the 'danger theory'.

IT Major Concepts
Biochemistry and Molecular Biophysics; Molecular Genetics (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis); Tumor Biology

IT Parts, Structures, & Systems of Organisms
T lymphocyte: blood and lymphatics, immune system; dendritic cells: adoptive transfer, autologous, immune system

IT Chemicals & Biochemicals
CD40L: gene transfer; **GM-CSF** [granulocyte-macrophage colony stimulating factor]: gene transfer; IL-12 [interleukin-12]; IL-6 [interleukin-6]; antigen presenting molecules; tumor antigens

IT Miscellaneous Descriptors
immune response; tumor-derived apoptotic bodies

RN 83869-56-1 (**GM-CSF**)
83869-56-1 (GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR)

L11 ANSWER 9 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:338830 BIOSIS
DN PREV200000338830
TI Reduction in serum IL-6 after **vaccination** of breast cancer patients with tumour-associated antigens is related to estrogen receptor status.
AU Jiang, Xian Peng (1); Yang, Ding Cheng; Elliott, Robert L.; Head, Jonathan F.
CS (1) Mastology Research Institute, 8221 Kelwood Avenue, Baton Rouge, LA, 70806 USA
SO Cytokine, (May, 2000) Vol. 12, No. 5, pp. 458-465. print.
ISSN: 1043-4666.
DT Article
LA English
SL English
AB Elevated serum IL-6 concentrations have been associated with poor prognosis in a variety of cancers, and decreases in serum IL-6 concentrations have been reported after chemotherapy. We have demonstrated that serum IL-6 concentrations are elevated in breast cancer patients (normal women 0.7 +- 2.5 pg/ml (n=36), breast cancer patients 38.3 +- 138.7 pg/ml (n=111)). After **vaccination** of breast cancer patients with a combination of tumour-associated antigens and biological adjuvants (IL-2 and **GM-CSF**), the concentration of IL-6 decreased significantly (P<0.05) to 8.1 +- 14.6 pg/ml (n=85). Other studies have shown that oestrogen suppresses IL-6 production in oestrogen receptor positive breast cancer cells. We have demonstrated that the decrease in IL-6 associated with **vaccination** is related to the oestrogen receptor status of the tumours from breast cancer patients, as a decrease in IL-6 from 124.0 +- 267.5 pg/ml (n=26) to 6.2 +- 11.0 pg/ml

(n=34) only occurs in patients with oestrogen receptor negative tumours. The IL-6 concentration in breast cancer patients with oestrogen receptor positive tumours remained unchanged (9.5 pg/ml before **vaccination**, and 9.3 pg/ml after **vaccination**). These results suggest that postmenopausal women with oestrogen receptor negative breast cancers, who do not respond well to either hormonal therapy with tamoxifen or adjuvant chemotherapy, may have a significant response to **vaccination** with autologous tumour-associated antigens.

IT Major Concepts
Clinical Endocrinology (Human Medicine, Medical Sciences); Clinical Immunology (Human Medicine, Medical Sciences); Gynecology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences)

IT Diseases
breast cancer: neoplastic disease, reproductive system disease/female

IT Chemicals & Biochemicals
GM-CSF [granulocyte-macrophage colony stimulating factor]: biological adjuvant, **vaccination**; IL-2 [interleukin-2]: biological adjuvant, **vaccination**; IL-6 [interleukin-6]: serum concentration; estrogen receptor: status; **tumor-associated antigens**: **vaccination**

IT Alternate Indexing
Breast Neoplasms (MeSH)

IT Methods & Equipment
vaccination: **immunization** method

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): female, patient, postmenopausal

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 83869-56-1 (**GM-CSF**)
83869-56-1 (GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR)

L11 ANSWER 10 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1999:357605 BIOSIS

DN PREV199900357605

TI Dendritic cells infiltrating tumors cotransduced with granulocyte/macrophage colony-stimulating factor (**GM-CSF**) and CD40 ligand genes take up and present endogenous **tumor-associated antigens**, and prime naive mice for a cytotoxic T lymphocyte response.

AU Chiodoni, Claudia; Paglia, Paola; Stoppacciaro, Antonella; Rodolfo, Monica; Parenza, Mariella; Colombo, Mario P. (1)

CS (1) Department of Experimental Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori, Via Venezian 1, 20133, Milan Italy

SO Journal of Experimental Medicine, (July 5, 1999) Vol. 190, No. 1, pp. 125-133.
ISSN: 0022-1007.

DT Article

LA English

SL English

AB We transduced BALB/c-derived C-26 colon carcinoma cells with granulocyte/macrophage colony-stimulating factor (**GM-CSF**) and CD40 ligand (CD40L) genes to favor interaction of these cells with host dendritic cells (DCs) and, therefore, cross-priming. Cotransduced

cells showed reduced tumorigenicity, and tumor take was followed by regression in some mice. In vivo tumors were heavily infiltrated with DCs that were isolated, phenotyped, and tested in vitro for stimulation of tumor-specific cytotoxic T lymphocytes (CTLs). BALB/c C-26 carcinoma cells express the endogenous murine leukemia virus (MuLV) env gene as a **tumor-associated antigen**. This **antigen** is shared among solid tumors of BALB/c and C57BL/6 mice and contains two epitopes, AH-1 and KSP, recognized in the context of major histocompatibility complex class I molecules H-2Ld and H-2Kb, respectively. DCs isolated from C-26/GM/CD40L tumors grown in (BALB/c X C57BL/6)F1 mice (H-2dXb) stimulated interferon gamma production by both anti-AH-1 and KSP CTLs, whereas tumor-infiltrating DCs (TIDCs) of BALB/c mice stimulated only anti-AH-1 CTLs. Furthermore, TIDCs primed naive mice for CTL activity as early as 2 d after injection into the footpad, whereas double-transduced tumor cells required at least 5 d for priming; this difference may reflect direct DC priming versus indirect tumor cell priming. Immunohistochemical staining indicated colocalization of DCs and apoptotic bodies in the tumors. These data indicate that DCs infiltrating tumors that produce **GM-CSF** and CD40L can capture cellular antigens, likely through uptake of apoptotic bodies, and mature in situ to a stage suitable for antigen presentation. Thus, tumor cell-based **vaccines** engineered to favor the interaction with host DCs can be considered.

IT Major Concepts
Cell Biology; Immune System (Chemical Coordination and Homeostasis); Tumor Biology

IT Parts, Structures, & Systems of Organisms
dendritic cells: immune system, tumor infiltrating; T lymphocytes: blood and lymphatics, cytotoxic, tumor-specific, immune system

IT Chemicals & Biochemicals
granulocyte-macrophage colony stimulating factor [**GM-CSF**]; **tumor-associated antigens**:
endogenous; CD40 ligand [CD40L]; mouse CD40L gene [CD40 ligand gene] (Muridae); mouse **GM-CSF** gene [granulocyte-macrophage colony stimulating factor gene] (Muridae); murine leukemia virus env gene (Retroviridae)

IT Methods & Equipment
retroviral-mediated gene transfer: DNA transfer method

IT Miscellaneous Descriptors
antigen presentation

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
mouse (Muridae): breed-BALB/c, breed-C57BL/6; C-26 cell line (Muridae):
Balb/c-derived colon carcinoma cells

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L11 ANSWER 11 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:272003 BIOSIS
DN PREV199900272003
TI Augmented anti-tumor immunity by **immunization** with epidermal cells infected with an adenovirus vector containing a cDNA for **GM**

-**CSF**.
AU Ozawa, H. (1); Seiffert, K. (1); Hackett, N. (1); Topf, N. (1); Crystal, R. G. (1); Granstein, R. D. (1)
CS (1) Department of Dermatol. and Div. of Pulmonary and Critical Care Medicine, Weill Medical College of Cornell University, New York, NY USA
SO Journal of Investigative Dermatology, (April, 1999) Vol. 112, No. 4, pp. 626.
Meeting Info.: 60th Annual Meeting of the Society for Investigative Dermatology Chicago, Illinois, USA May 5-9, 1999
ISSN: 0022-202X.
DT Conference
LA English
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Tumor Biology
IT Parts, Structures, & Systems of Organisms
epidermal cells: **antitumor** immunity augmentation, granulocyte-macrophage colony stimulating factor complementary DNA transfection, **tumor-associated antigen** presentation, integumentary system
IT Diseases
cancer: immune gene therapy, neoplastic disease
IT Alternate Indexing
Neoplasms (MeSH)
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Adenoviridae: Animal Viruses, Viruses, Microorganisms; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
adenovirus (Adenoviridae): gene vector; mouse (Muridae): animal model
ORGN Organism Superterms
Animal Viruses; Animals; Chordates; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates; Viruses

L11 ANSWER 12 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:264295 BIOSIS
DN PREV199900264295
TI IL-13 can substitute for IL-4 in the generation of dendritic cells for the induction of cytotoxic T lymphocytes and gene therapy.
AU Alters, Susan E. (1); Gadea, Jose R.; Holm, Bari; Lebkowski, Jane; Philip, Ramila
CS (1) Surromed Inc., 1060 E. Meadow Cir., Palo Alto, CA, 94303 USA
SO Journal of Immunotherapy, (May, 1999) Vol. 22, No. 3, pp. 229-236.
DT Article
LA English
SL English
AB **Immunization** with **tumor-associated antigen** pulsed dendritic cells (DC) has been shown to elicit both protective and therapeutic **antitumor** immunity in a variety of animal models and is currently being investigated for the treatment of cancer patients in clinical trials. In this study we show that DC can be generated from peripheral blood mononuclear cells of healthy donors as well as breast and melanoma cancer patients using granulocyte-macrophage colony-stimulating factor (**GM-CSF**) and interleukin-13

(IL-13) and that these DC have many of the same characteristics as DC differentiated using **GM-CSF** and EL-4. The DC generated in **GM-CSF** and IL-13 are CD14- and express high levels of the cell surface markers CD86, HLA-DR, and CD58, as do DC generated in **GM-CSF** and IL-4. The purity and yield of both DC populations are not significantly different. Furthermore, both populations of DC are effective at presentation of alloantigen as determined in a mixed lymphocyte response, and both are able to process and present soluble tetanus toxoid antigen to CD4+ T cells. Because we are interested in the generation of DC for antigen-specific cytotoxic T lymphocyte (CTL) generation, we compared the ability of peptide-pulsed DC differentiated in **GM-CSF** and IL-4 versus **GM-CSF** and IL-13 for the generation of influenza and MART-1 specific CTL. Both populations of DC induced CD3+CD8+CD4- and CD56- CTL, which could lyse the appropriate targets in an antigen-specific manner. Finally, both **GM-CSF** and IL-4 DC and **GM-CSF** and IL-13 DC yielded similar beta galactosidase expression levels after transduction with recombinant adenovirus containing the LacZ gene. These results suggest that DC generated in **GM-CSF** and IL-13 may be useful for immunotherapy and gene therapy protocols.

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis); Molecular Genetics (Biochemistry and Molecular Biophysics); Pharmacology

IT Parts, Structures, & Systems of Organisms
cytotoxic T lymphocyte: antigen specific, immune system, blood and lymphatics, generation; dendritic cell: immune system; **tumor-associated antigen** pulsed dendritic cell: immune system, immunostimulant

IT Chemicals & Biochemicals
beta galactosidase: expression; granulocyte-macrophage colony stimulating factor: progenitor; interleukin-13: progenitor; interleukin-4: progenitor; CD86: cell surface marker; adenovirus LacZ gene (Adenoviridae)

IT Methods & Equipment
gene therapy: recombinant gene expression applications, therapeutic method; **immunization: immunization** method

ORGN Super Taxa
Adenoviridae: Animal Viruses, Viruses, Microorganisms

ORGN Organism Name
adenovirus (Adenoviridae)

ORGN Organism Superterms
Animal Viruses; Microorganisms; Viruses

RN 9031-11-2 (BETA GALACTOSIDASE)

L11 ANSWER 13 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1999:250770 BIOSIS

DN PREV199900250770

TI Cytotoxic T lymphocyte response against non-immunoselected tumor antigens predicts the outcome of gene therapy with IL-12-transduced tumor cell **vaccine.**

AU Rodolfo, M. (1); Zilocchi, C.; Cappetti, B.; Parmiani, G.; Melani, C.; Colombo, M. P.

CS (1) Experimental Oncology D, Istituto Nazionale Tumori, via Venezian,

1-20133, Milan Italy
SO Gene Therapy, (May, 1999) Vol. 6, No. 5, pp. 865-872.
ISSN: 0969-7128.
DT Article
LA English
SL English
AB The colon adenocarcinoma C26, carrying two endogenous **tumor-associated antigens** (TAA) recognized by CTL, has been transduced with the gene coding for the human folate receptor alpha (FRalpha) as an additional antigen in order to study the efficacy of **vaccination** against a tumor expressing multiple antigens. A dicistronic vector was used to transduce the IL-12 genes to create C26/IL-12/FRalpha that has been used as a cellular **vaccine** to treat mice bearing lung metastases of C26/FRalpha. After **vaccination** mice were partially splenectomized and splenic lymphocytes frozen and used retrospectively to study in vitro CD8 T cell response related to the treatment outcome. **Vaccination** cured 50% of mice and the effect was CD8 T cell dependent. Mice either cured (responders) or not cured (nonresponders) by **vaccination** developed tumor-specific CTL. However, analysis of CTL specificity and pCTL frequencies revealed that responders had a predominant CTL activity against endogenous C26-related tumor antigens, whereas nonresponders had CTL that recognized preferentially the FRalpha antigen. CD8 from responder mice were characterized to release high levels of granulocyte-macrophage (**GM**)**-CSF** upon antigen stimulation. Tumors obtained from mice that died despite **vaccination** lost expression of the FRalpha transgene but maintained expression of endogenous C26 antigens. Immuno-selection against FRalpha antigen was not observed in tumors from non-**vaccinated** controls and from CD8-depleted **vaccinated** mice. Down-regulation of FRalpha antigen expression was due, at least in part, to methylation of retroviral vector long terminal repeat promoter since FRalpha expression was partially restored, ex vivo, by treatment with 5-aza-2'-deoxy-cytidine (aza). These results indicate that CD8 T cell-mediated immunoselection and production of **GM-CSF** are determining factors for the efficacy of tumor **vaccines**.
IT Major Concepts
Genetics; Immune System (Chemical Coordination and Homeostasis); Tumor Biology
IT Parts, Structures, & Systems of Organisms
cytotoxic T lymphocyte: blood and lymphatics, immune system
IT Chemicals & Biochemicals
non-immunoselected tumor antigens: cytotoxic T lymphocyte response
IT Methods & Equipment
interleukin-12-transduced tumor cell **vaccine**: gene therapeutic method, immunologic method
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae); C26 cell line (Muridae): murine colon adenocarcinoma cells
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L11 ANSWER 14 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1999:87705 BIOSIS
DN PREV199900087705
TI Hyper-IL-6, a fusion protein of IL-6 and IL-6-receptor, promotes together with stem cell factor (SCF) and **GM-CSF** the expansion of functional dendritic cells from CD34+ hematopoietic progenitor cells.
AU Bernhard, Helga (1); Metzger, Jochen (1); Nicklisch, Nicole (1); Rose-John, Stefan; Peschel, Christian (1)
CS (1) III. Med. Klin., Klin. Rechts Isar Technischen Univ. Muenchen, Muenchen Germany
SO Annals of Hematology, (1998) Vol. 77, No. SUPPL. 2, pp. S41.
Meeting Info.: Annual Congress of the German and Austrian Societies of Hematology and Oncology Frankfurt, Germany October 25-28, 1998 Austrian Society of Hematology and Oncology
. ISSN: 0939-5555.
DT Conference
LA English
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Immune System (Chemical Coordination and Homeostasis); Tumor Biology
IT Parts, Structures, & Systems of Organisms
dendritic cells: functional, immune system, **vaccine** adjuvant; CD34 positive hematopoietic progenitor cells: blood and lymphatics; T cells: blood and lymphatics, immune system
IT Chemicals & Biochemicals
c-kit; gp130 [glycoprotein 130]; stem cell factor; **GM-CSF** [granulocyte-macrophage colony stimulating factor]; Hyper-IL-6 [Hyper-interleukin-6]: fusion protein; HER-2/neu: **tumor-associated antigen**; IL-6 receptor [interleukin-6 receptor]; IL-6 [interleukin-6]
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 42013-48-9 (GP130)

L11 ANSWER 15 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:457783 BIOSIS
DN PREV199800457783
TI DNA as **vaccine** or therapeutic against cancer and viral infections.
AU Moelling, K. (1); Pavlovic, J.; Schultz, J.; Nawrath, M.; Petrzilka, D.
CS (1) Inst. Med. Virol., Univ. Zurich, Gloriastrasse 30, CH-8028 Zurich Switzerland
SO Journal of Molecular Medicine (Berlin), (May, 1998) Vol. 76, No. 6, pp. B17.
Meeting Info.: 2nd Congress of Molecular Medicine Berlin, Germany May 6-9,
1998
ISSN: 0946-2716.
DT Conference
LA English
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Infection; Tumor

Biology
IT Diseases
malignant melanoma: neoplastic disease
IT Chemicals & Biochemicals
gp100/pmel17: melanoma-**associated tumor antigen**; plasmid DNA: **vaccine**; B7.1: costimulator; **GM-CSF** [granulocyte-macrophage colony stimulating factor]; IL-12 [interleukin-12]; IL-2 [interleukin-2]
IT Miscellaneous Descriptors
protective immune response; Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae): model
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L11 ANSWER 16 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:314444 BIOSIS
DN PREV199800314444
TI The role of tumor necrosis factor alpha in modulating the quantity of peripheral blood-derived, cytokine-driven human dendritic cells and its role in enhancing the quality of dendritic cell function in presenting soluble antigens to CD4+ T cells in vitro.
AU Chen, Bing-Guan; Shi, Yijun; Smith, Jeffrey D.; Choi, David; Geiger, James D.; Mule, James J. (1)
CS (1) Dep. Surg., Univ. Mich. Med. Cent., 1520c MSRB-1, 1150 W. Medical Center Dr., Ann Arbor, MI 48109-0666 USA
SO Blood, (June 15, 1998) Vol. 91, No. 12, pp. 4652-4661.
ISSN: 0006-4971.
DT Article
LA English
AB Because dendritic cells (DC) are critically involved in both initiating primary and boosting secondary host immune responses, attention has focused on the use of DC in **vaccine** strategies to enhance reactivity to **tumor-associated antigens**. We have reported previously the induction of major histocompatibility complex class II-specific T-cell responses after stimulation with tumor antigen-pulsed DC in vitro. The identification of in vitro conditions that would generate large numbers of DC with more potent antigen-presenting cell (APC) capacity would be an important step in the further development of clinical cancer **vaccine** approaches in humans. We have focused attention on identifying certain exogenous cytokines added to DC cultures that would lead to augmented human DC number and function. DC progenitors from peripheral blood mononuclear cells (PBMC) were enriched by adherence to plastic, and the adherent cells were then cultured in serum-free XVIVO-15 medium (SFM) for 7 days with added granulocyte-macrophage colony-stimulating factor (**GM-CSF**) and interleukin-4 (IL-4). At day 7, cultures contained cells that displayed the typical phenotypic and morphologic characteristics of DC. Importantly, we have found that the further addition of tumor necrosis factor alpha (TNFalpha) at day 7 resulted in a twofold higher yield of DC compared with non-TNFalpha-containing DC cultures at day 14. Moreover, 14-day cultured

DC generated in the presence of TNFalpha (when added at day 7) demonstrated marked enhancement in their capacity to stimulate a primary allogeneic mixed leukocyte reaction (8-fold increase in stimulation index (SI)) as well as to present soluble tetanus toxoid and candida albicans (10- to 100-fold increases in SI) to purified CD4+ T cells. These defined conditions allowed for significantly fewer DC and lower concentrations of soluble antigen to be used for the pulsing of DC to efficiently trigger specific T-cell proliferative responses in vitro. When compared with non-TNFalpha-supplemented cultures, these DC also displayed an increased surface expression of CD83 as well as the costimulatory molecules, CD80 and CD86. Removal of TNFalpha from the DC cultures after 2 or 4 days reduced its enhancing effect on DC yield, phenotype, and function. Thus, the continuous presence of TNFalpha over a 7-day period was necessary to achieve the maximum enhancing effect observed. Collectively, our findings point out the importance of exogenous TNFalpha added to cultures of cytokine-driven human DC under serum-free conditions, which resulted in an enhanced number and function of these APC. On the basis of these results, we plan to initiate clinical **vaccine** trials in patients that use tumor-pulsed DC generated under these defined conditions.

IT Major Concepts
Blood and Lymphatics (Transport and Circulation)
IT Parts, Structures, & Systems of Organisms
dendritic cell: immune system; peripheral blood mononuclear cell: blood and lymphatics, immune system; CD4-positive T cell: blood and lymphatics, cytokine driven, immune system
IT Chemicals & Biochemicals
soluble antigens; tumor necrosis factor-alpha
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L11 ANSWER 17 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:306446 BIOSIS
DN PREV199800306446
TI Pulsing of dendritic cells with cell lysates from either B16 melanoma or MCA-106 fibrosarcoma yields equally effective **vaccines** against B16 tumors in mice.
AU Dematos, Pierre (1); Abdel-Wahab, Zeinab; Vervaert, Carol; Hester, Dina; Seigler, Hilliard
CS (1) Box 3966, Duke Univ. Med. Cent., Erwin Rd., Durham, NC 27710 USA
SO Journal of Surgical Oncology, (June, 1998) Vol. 68, No. 2, pp. 79-91. ISSN: 0022-4790.
DT Article
LA English
AB Background and Objectives: Dendritic cells (DC) pulsed in vitro with a variety of antigens have proved effective in producing specific **antitumor** effects in vivo. Experimental evidence from other laboratories has confirmed that shared antigens can be encountered in histologically distinct tumors. In our experiments, we set out to evaluate the immunotherapeutic potential of **vaccines** consisting of DC pulsed with MCA-106 fibrosarcoma or B16 melanoma cell lysates and to

determine whether a crossreactivity exists between the two tumors. Methods: DC were prepared from the bone marrow of C57BL/6 (B6) mice by culturing progenitor cells in murine granulocyte-macrophage colony-stimulating factor (**GM-CSF**). They were separated into three equal groups and were either pulsed with B16 melanoma cell lysates (BDC), pulsed with tumor extract from the syngeneic fibrosarcoma MCA106 (MDC), or left unpulsed (UDC). DC were then used to **immunize** three groups of mice, with all mice receiving two weekly intravenous (IV) doses of 1 X 106 DC from their respective preparations on days -14 and -7. A fourth group of control mice were left untreated. On day 0, all mice were challenged with subcutaneous injections of 1 X 105 B16 and 1 X 105 MCA tumor cells, administered in the left and right thighs, respectively. After the inoculations, the mice were monitored closely with respect to tumor growth and survival. Results: The MDC mice developed specific cellular immunity directed against not only MCA-106 tumor cells, but also against B 16 melanoma, as measured through chromium-release assays of splenocyte preparations, while remaining ineffective at killing both L929 fibroblasts and CT26 tumor cells. By day 30 after tumor inoculations, control mice manifested the largest B16 tumor volumes at a mean of 2185 mm3, followed by the UDC, MDC, and BDC groups at 92 mm3 (P = 0.00008), 3 mm3 (P = 0.000002), and 2 mm3 (p = 0.00004), respectively. The survival data mirrored this pattern, with control animals displaying the shortest mean survival time (37.1 +- 4.0 days), followed by UDC (44.8 +- 6.6), MDC (56.2 +- 14.7), and BDC (56.4 +- 18.3) animals. No significant differences were noted between MCA-106 and B16 cell lysate-pulsed DC **vaccines** with respect to their abilities to inhibit B16 tumor growth and to prolong survival. These findings were confirmed using a B16 pulmonary metastasis model. Likewise, **vaccination** with interferon-gamma gene-modified MCA-106 tumor cells was shown to be effective at protecting against a subsequent subcutaneous B 16 tumor challenge in 3 of 4 mice observed. Conclusions: These results demonstrate that **immunization** with antigen-pulsed DC confers cellular immunity, retards tumor growth, and prolongs the survival of tumor-challenged mice. The ability of MCA-106 cell lysate-pulsed DC **vaccines** to inhibit the growth of subcutaneous B16 tumors also suggests the presence of shared **tumor-associated antigens** between these two histologically distinct tumors.

IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Tumor Biology

IT Parts, Structures, & Systems of Organisms
dendritic cells: immune system

IT Diseases
fibrosarcoma: neoplastic disease; melanoma: neoplastic disease

IT Chemicals & Biochemicals
granulocyte-macrophage colony stimulating factor: cell culture medium

IT Methods & Equipment
antitumor immunotherapy: therapeutic method

IT Miscellaneous Descriptors
antigen-pulsed dendritic cells: **vaccine**; cellular immunity

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

B16 (Muridae): melanoma cells; C57BL/6 mouse (Muridae); MCA-106 (Muridae): fibrosarcoma cells

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L11 ANSWER 18 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:168573 BIOSIS
DN PREV199800168573
TI **Vaccination** of melanoma patients with peptide- or tumor lysate-pulsed dendritic cells.
AU Nestle, Frank O.; Alijagic, Selma; Gilliet, Michel; Sun, Yuansheng; Grabbe, Stephan; Dummer, Reinhard; Burg, Guenter; Schadendorf, Dirk (1)
CS (1) Clin. Coop. Unit Dermatooncol., Klinikum Mannheim, Univ. Heidelberg, Theodor Kutzer Ufer 1, 68135 Mannheim Germany
SO Nature Medicine, (March, 1998) Vol. 4, No. 3, pp. 328-332. ISSN: 1078-8956.
DT Article
LA English
AB Melanoma is the main cause of death in patients with skin cancer. Cytotoxic T lymphocytes (CTLs) attack melanoma cells in an HLA-restricted and tumor antigen-specific manner. Several melanoma-**associated tumor antigens** have been identified. These antigens are suitable candidates for a **vaccination** therapy of melanoma. Dendritic cells (DCs) are antigen-presenting cells (APCs) specialized for the induction of a primary T-cell response. Mouse studies have demonstrated the potent capacity of DCs to induce **antitumor** immunity. In the present clinical pilot study, DCs were generated in the presence of granulocyte/macrophage-colony stimulating factor (**GM -CSF**) and interleukin 4 (IL-4) and were pulsed with tumor lysate or a cocktail of peptides known to be recognized by CTLs, depending on the patient's HLA haplotype. Keyhole limpet hemocyanin (KLH) was added as a CD4 helper antigen and immunological tracer molecule. Sixteen patients with advanced melanoma were **immunized** on an outpatient basis. **Vaccination** was well tolerated. No physical sign of autoimmunity was detected in any of the patients. DC **vaccination** induced delayed-type hypersensitivity (DTH) reactivity toward KLH in all patients, as well as a positive DTH reaction to peptide-pulsed DCs in 11 patients. Recruitment of peptide-specific CTLs to the DTH challenge site was also demonstrated. Therefore, antigen-specific immunity was induced during DC **vaccination**. Objective responses were evident in 5 out of 16 evaluated patients (two complete responses, three partial responses) with regression of metastases in various organs (skin, soft tissue, lung, pancreas) and one additional minor response. These data indicate that **vaccination** with autologous DCs generated from peripheral blood is a safe and promising approach in the treatment of metastatic melanoma. Further studies are necessary to demonstrate clinical effectiveness and impact on the survival of melanoma patients.
IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
dendritic cells: tumor lysate-pulsed, peptide-pulsed, immune system

IT Diseases
melanoma: neoplastic disease, metastatic
IT Chemicals & Biochemicals
granulocyte-macrophage colony stimulating factor; interleukin-4; keyhole limpet hemocyanin; HLA: types
IT Methods & Equipment
vaccination: therapeutic method, immunologic method
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L11 ANSWER 19 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:539344 BIOSIS
DN PREV199799838547
TI Development of cancer **vaccines** and anti-cancer therapeutics drug delivery systems using poly-B-1-greater 4-N acetyl glucosamine.
AU Vournakis, J. N. (1); Weisberg, T.; Brown, J. (1); Demcheva, M. (1); Woo, S. (1); Broderick, C. (1); Cole, D. (1)
CS (1) Center Molecular Structural Biol., Hollings Cancer Center, Med. Univ. South Carolina, 171 Ashley Ave., Charleston, SC 29425 USA
SO International Journal of Oncology, (1997) Vol. 11, No. SUPPL., pp. 929. Meeting Info.: 2nd World Congress on Advances in Oncology Athens, Greece October 16-18, 1997
ISSN: 1019-6439.
DT Conference; Abstract
LA English
IT Major Concepts
Animal Care; Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Clinical Immunology (Human Medicine, Medical Sciences); Endocrine System (Chemical Coordination and Homeostasis); Hematology (Human Medicine, Medical Sciences); Immune System (Chemical Coordination and Homeostasis); Metabolism; Methods and Techniques; Oncology (Human Medicine, Medical Sciences); Pathology; Pharmacology
IT Chemicals & Biochemicals
ACETYL GLUCOSAMINE; GLUCOSAMINE
IT Miscellaneous Descriptors
ANIMAL MODEL; ANTI-CANCER THERAPEUTIC DRUG DELIVERY SYSTEMS; ANTIGEN-PRESENTING CELLS; CANCER; CLASS I MAJOR HISTOCOMPATIBILITY COMPLEX-RESTRICTED EPITOPES; CYTOKINE; C57BL/6 MOUSE; DEVELOPMENT;
DRUG
DELIVERY METHOD; **GM-CSF**; GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR; IMMUNE SYSTEM; JRT22 CELL LINE; MART-1-(27-35) PEPTIDE; MART-1-(27-35)-SPECIFIC JURKAT T CELLS; NEOPLASTIC DISEASE; PEPTIDE-BASED CANCER **VACCINES**; PHARMACEUTICALS; POLY-B-1-4-N-ACETYL GLUCOSAMINE; SCID MOUSE; SEVERE COMBINED IMMUNODEFICIENCY MOUSE; **TUMOR-ASSOCIATED ANTIGENS**; **VACCINE**
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae:
Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Hominidae (Hominidae); Muridae (Muridae)

ORGN Organism Superterms
animals; chordates; humans; mammals; nonhuman mammals; nonhuman vertebrates; primates; rodents; vertebrates
RN 7512-17-6 (ACETYL GLUCOSAMINE)
3416-24-8 (GLUCOSAMINE)

L11 ANSWER 20 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:253000 BIOSIS
DN PREV199799552203
TI Granulocyte-macrophage colony-stimulating factor as an adjuvant in tumor immunotherapy.
AU Fagerberg, Jan
CS Dep. Oncol. Immunol. Res. Lab., Karolinska Hosp., S-171-76 Stockholm Sweden
SO Medical Oncology (London), (1996) Vol. 13, No. 3, pp. 155-160.
ISSN: 1357-0560.
DT General Review
LA English
AB Induction of specific anti-tumor immunity by active **immunization** has been the aim of researchers for decades. However, a generally applicable successful **immunization** strategy that could be used in the clinic has not yet been devised. Recent research has been directed at identifying and defining tumor-specific and **tumor-associated antigens**. Several good candidates are now at hand. If these antigens are to perform optimally at **immunization** , there is a need for proper adjuvants. This article focuses on one adjuvant, the cytokine granulocyte-macrophage colony-stimulating factor (**GM-CSF**), and the possible application of this molecule to active specific immunotherapy.
IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences); Endocrine System (Chemical Coordination and Homeostasis); Oncology (Human Medicine, Medical Sciences); Pharmacology
IT Miscellaneous Descriptors
ANTINEOPLASTIC-DRUG; CANCER; GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR; IMMUNOLOGIC-DRUG; IMMUNOTHERAPY; NEOPLASTIC DISEASE; ONCOLOGY; PATIENT; PHARMACOLOGY
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

L11 ANSWER 21 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1996:155043 BIOSIS
DN PREV199698727178
TI Selected strategies to augment polynucleotide **immunization**.
AU Conry, R. M. (1); Widera, G.; Lobuglio, A. F.; Fuller, J. T.; Moore, S. E.; Barlow, D. L.; Turner, J.; Yang, N.-S.; Curiel, D. T.
CS (1) LB Wallace Tumor Inst., 1824 6th Ave. South, Univ. Alabama Birmingham,
Birmingham, AL 35294-3300 USA
SO Gene Therapy, (1996) Vol. 3, No. 1, pp. 67-74.
ISSN: 0969-7128.
DT Article
LA English

AB We sought to amplify the immune response to polynucleotide **immunization** through co-delivery of complementary DNA (cDNA) encoding a cytokine or co-stimulatory molecule to enhance antigen presentation. In the context of intramuscular **immunization**, we examined co-delivery of cDNAs for B7-1 and human carcinoembryonic antigen (CEA) within separate plasmids or a dual plasmid with two independent expression cassettes. Intramuscular delivery of the dual expression plasmid produced anti-CEA antibody responses and **antitumor** effects superior to those generated by plasmid DNA encoding CEA alone. However, co-delivery of cDNAs encoding B7-1 and CEA in the form of two separate plasmids produced no augmentation. The importance of single plasmid delivery suggests the effectiveness of this strategy is contingent upon co-expression of B7-1 and CEA within the same cell. The success of cutaneous polynucleotide **immunization** by particle bombardment is thought to derive largely from the presence of Langerhans cells within the skin. we hypothesized that co-delivery of plasmid DNA encoding granulocyte-macrophage colony stimulating factor (**GM-CSF**) by particle bombardment would enhance the antigen presenting capacity of Langerhans cells at the inoculation site similar to its effects in vitro. Augmentation of CEA-specific lymphoblastic transformation and antibody response was observed when plasmid **GM-CSF** (pGM-CSF) was administered 3 days prior to each dose of plasmid DNA encoding CEA. These strategies for augmentation of immune response to polynucleotide **immunization** should be applicable to a wide variety of antigenic targets including infectious agents and other **tumor-associated antigens.**

IT Major Concepts
Cell Biology; Genetics; Immune System (Chemical Coordination and Homeostasis); Metabolism; Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics); Tumor Biology

IT Miscellaneous Descriptors
B7-1; CANCER THERAPY RELEVANCE; CARCINOEMBRYONIC ANTIGEN; COMPLEMENTARY DNA; CUTANEOUS POLYNUCLEOTIDE **IMMUNIZATION**; DNA TRANSFER METHOD; GENE GUN; GENETIC ENGINEERING; GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR; LANGERHANS CELL; PARTICLE BOMBARDMENT

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
mouse (Muridae)

ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates

L11 ANSWER 22 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1996:77289 BIOSIS
DN PREV199698649424
TI Murine dendritic cells loaded in vitro with soluble protein prime cytotoxic T lymphocytes against tumor antigen in vivo.
AU Paglia, Paola (1); Chiodoni, Claudia; Rodolfo, Monica; Colombo, Mario P.
CS (1) Div. Exp. Oncol. D, Ist. Nazionale per lo Studio e la Cura dei Tumori, Via Venezian 1, 20133 Milano Italy
SO Journal of Experimental Medicine, (1996) Vol. 183, No. 1, pp. 317-322.

ISSN: 0022-1007.
DT Article
LA English
AB The Priming of an immune response against a major histocompatibility complex class I-restricted antigen expressed by nonhematopoietic cells involves the transfer of that antigen to a host bone marrow-derived antigen presenting cell (APC) for presentation to CD8+ T lymphocytes. Dendritic cells (DC), as bone marrow-derived APC, are first candidates for presentation of **tumor associated antigens** (TAA). The aim of this study was to see whether DC are able to prime in vivo antigen-specific cytotoxic T lymphocytes after exposure to a soluble protein antigen in vitro. Lacking a well-defined murine TAA, we took advantage of beta-galactosidase (beta-gal)transduced tumor cell lines as a model in which beta-gal operationally functions as TAA. For in vivo priming both a DC line, transduced or not transduced with the gene coding for murine **GM-CSF**, and fresh bone marrow-derived DC (bm-DC), loaded in vitro with soluble beta-gal, were used. Priming with either granulocyte macrophage colony-stimulating factor-transduced DC line or fresh bm-DC but not with untransduced DC line generated CTL able to lyse beta-gal-transfected target cells. Furthermore, **GM-CSF** was necessary for the DC line to efficiently present soluble beta-gal as an H-2L-d-restricted peptide to a beta-gal-specific CTL clone. Data also show that a long-lasting immunity against tumor challenge can be induced using beta-gal-pulsed bm-DC as **vaccine**. These results indicate that effector cells can be recruited and activated in vivo by antigen-pulsed DC, providing an efficient immune reaction against tumors.
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Development; Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis); Tumor Biology
IT Miscellaneous Descriptors
ANTIGEN-PRESENTING CELL; BETA-GALACTOSIDASE-TRANSDUCED TUMOR CELL LINE; EFFECTOR CELL; GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR; MAJOR HISTOCOMPATIBILITY COMPLEX CLASS I; **VACCINE**
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Muridae (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals; rodents; vertebrates

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AN 1992:503947 BIOSIS
DN BA94:122472
TI TUMOR ANTIGEN PRESENTATION BY EPIDERMAL ANTIGEN-PRESENTING CELLS IN THE MOUSE MODULATION BY GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR TUMOR

NECROSIS FACTOR ALPHA AND ULTRAVIOLET RADIATION.
AU GRABBE S; BRUVERS S; LINDGREN A M; HOSOI J; TAN K C; GRANSTEIN R D
CS MASS. GEN. HOSP., MGH-EAST, CUTANEOUS BIOL. RES. CENT., 13TH ST., CHARLESTOWN, MASS. 02129.
SO J LEUKOCYTE BIOL, (1992) 52 (2), 209-217.
CODEN: JLBIE7. ISSN: 0741-5400.
FS BA; OLD
LA English
AB I-A+ epidermal antigen-presenting cells (APCs, Langerhans cells) have been shown to present **tumor-associated antigens** (TAAs) and to induce tumor immunity in vivo. This study examined the effects of ultraviolet radiation (UVR) and the cytokines granulocyte-macrophage colony-stimulating factor (**GM-CSF**) and tumor necrosis factor .alpha. (TNF-.alpha.) on the ability of epidermal cells (ECs) to induce or to elicit immunity against the murine spindle cell tumor S1509a. Naive syngeneic mice were **immunized** three times at weekly intervals with ECs that had been cultured in **GM-CSF** for 18 h and then pulsed with TAA derived from S1509a. This resulted in protective immunity against subsequent tumor challenge, providing a model to study the conditions required for sensitization against TAAs by epidermal APCs. Culture of ECs in **GM-CSF** was required for induction of significant protective tumor immunity, and UV irradiation or incubation in TNF-.alpha. for 2 h after **GM-CSF** incubation abrogated the immunostimulatory effect of **GM-CSF**. However, unlike UVR, TNF-.alpha. did not significantly inhibit the induction of immunity when ECs were exposed to TNF-.alpha. before overnight incubation in **GM-CSF**, together with **GM-CSF**, or after pulsing with TAA, and anti-TNF-.alpha. antibody treatment did not abrogate the effects of UVR on this system. Furthermore, TNF-.alpha. incubation of ECs augmented their ability to elicit delayed-type hypersensitivity (DTH) and also enhanced elicitation of DTH by **GM-CSF**-cultured ECs, whereas UV-irradiation reduced it in a dose-dependent fashion. Taken together, these results demonstrate that **GM-CSF**, TNF-.alpha. and UVR are significant regulators of tumor antigen presentation by epidermal APCs and that the effects of the cytokines examined differ with regard to induction or elicitation of immunity.
IT Miscellaneous Descriptors
PROTECTIVE IMMUNITY DELAYED TYPE HYPERSENSITIVITY SKIN CANCER UV

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AN 1989:315045 BIOSIS
TI **GM-CSF** ENHANCES 3F8 MONOCLONAL ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY AGAINST HUMAN MELANOMA AND NEUROBLASTOMA.
AU KUSHNER B H; CHEUNG N-K V
CS DEP. PEDIATR., MEML. SLOAN-KETTERING CANCER CENT., 1275 YORK AVE., NEW YORK, N.Y. 10021.
SO BLOOD, (1989) 73 (7), 1936-1941.
CODEN: BLOOAW. ISSN: 0006-4971.
FS BA; OLD
LA English
AB 3F8 is a murine monoclonal IgG3 antibody specific for the **tumor-associated antigen** ganglioside GD2. Previous in vitro studies suggest that tumor regressions observed in a phase I clinical trial of 3F8 may be attributable to complement activation by 3F8 and to

3F8-dependent cellular cytotoxicity (ADCC) with lymphocytes. We now describe 3F8-mediated ADCC of GD2-positive tumor targets (melanoma and neuroblastoma) with human granulocytes and report that recombinant human granulocyte-macrophage colony-stimulating factor (**GM-CSF**) enhanced this phenomenon. Cytotoxicity required binding of 3F8 to the low-affinity Fc receptor type III (CD16) on the granulocytes and was poor with tumor-binding monoclonal antibodies of other immunolgobulin (ie. non-IgG3) subclasses, **GM-CSF** (2 to 20 ng/mL) increased ADCC by 93% to 26% at limiting dilutions of 3F8 (1 .mu.g/mL). With most GD2-positive cell lines tested, this effect translated into a tenfold or greater augmentation in 3F8 efficiency at mediating ADCC. Comparable enhancement occurred whether **GM-CSF** was present in the ADCC assay or granulocytes were incubated with **GM-CSF** and washed before the assay. Nonoxidative mechanisms may be important for ADCC since 3F8 mediated ADCC with granulocytes from two children with chronic granulomatous disease; this cytotoxicity was also enhanced by **GM-CSF**. Since **GM-CSF** induces a neutrophilia in patients, our data suggest that this cytokine may have the potential of amplifying 3F8 **antitumor** activity in patients by increasing effector cell numbers and by priming granulocytes for greater cytotoxicity.

IT Miscellaneous Descriptors
HUMAN IMMUNOLOGIC-DRUG ANTINEOPLASTIC-DRUG GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR COMPLEMENT ACTIVATION